

(10) **Patent No.:** US 9,315,635 B2  
(45) **Date of Patent:** \*Apr. 19, 2016

(52) U.S. Cl.

CPC ..... **C08G 77/458** (2013.01); **A61F 2/04**  
(2013.01); **A61M 39/22** (2013.01); **C08G**  
**18/5096** (2013.01); **C08G 18/61** (2013.01);  
**C08G 18/6535** (2013.01); **C08G 77/388**  
(2013.01); **C08G 77/445** (2013.01); **C08G**  
**77/448** (2013.01); **C08G 77/46** (2013.01);  
**C08L 83/10** (2013.01); **C08G 2101/0008**  
(2013.01); **C08G 2101/0083** (2013.01)

(58) **Field of Classification Search**  
None  
See application file for complete search history.

(56) **References Cited**

U.S. PATENT DOCUMENTS

3,246,048	A	4/1966	Haluska
4,384,976	A	5/1983	Grunert et al.

(Continued)

FOREIGN PATENT DOCUMENTS

EP	0252878	A1	1/1988
EP	1707583	A1	10/2006

(Continued)

## OTHER PUBLICATIONS

English translation of an Office Action; “Notice of Rejection,” issued by the Japanese Patent Office on Aug. 7, 2013, which corresponds to Japanese Patent Application No. 2011-514192 and is related to U.S. Appl. No. 13/968,685.

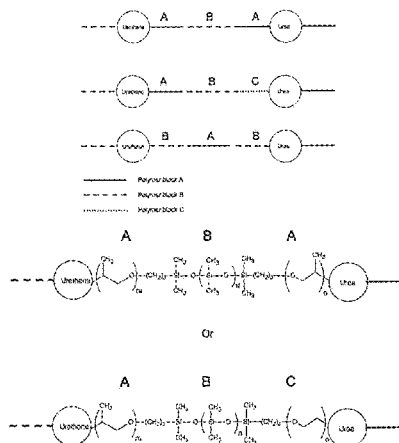
(Continued)

*Primary Examiner* — Marc Zimmer

(74) *Attorney, Agent, or Firm* — Studebaker & Brackett PC

(Continued)

**4 Claims, 8 Drawing Sheets**



(51) **Int. Cl.**

**C08G 18/65** (2006.01)  
**C08G 77/388** (2006.01)  
**C08L 83/10** (2006.01)  
**A61F 2/04** (2013.01)  
**C08G 101/00** (2006.01)

## FOREIGN PATENT DOCUMENTS

JP S42-14478 B 8/1967  
 JP S63-23930 A 2/1988  
 JP H10-60117 A 3/1998  
 JP H11-279950 A 10/1999  
 JP 2006-511680 A 4/2006  
 JP 2006-283025 A 10/2006  
 JP 2008-174749 A 7/2008  
 WO 2007/121180 A2 10/2007

## (56)

**References Cited**

## U.S. PATENT DOCUMENTS

4,663,413 A \* 5/1987 Ward et al. .... 528/26  
 5,200,436 A \* 4/1993 Kumar et al. .... 522/57  
 5,235,003 A 8/1993 Ward et al.  
 5,629,133 A \* 5/1997 Wolf et al. .... 430/269  
 5,660,819 A 8/1997 Tsubaki et al.  
 6,346,553 B1 \* 2/2002 LeGrow et al. .... 516/55  
 7,834,082 B2 11/2010 Haider et al.  
 2004/0014907 A1 \* 1/2004 Nowak et al. .... 525/474  
 2004/0254256 A1 12/2004 Lockwood et al.  
 2006/0155051 A1 7/2006 Herzig  
 2006/0223969 A1 10/2006 Roesler et al.  
 2008/0014166 A1 \* 1/2008 Klug et al. .... 424/70.12  
 2008/0075683 A1 3/2008 Herzig et al.

## OTHER PUBLICATIONS

International Search Report; PCT/IE2009/000038; Oct. 22, 2009.  
 Written Opinion; PCT/IE2009/000038; Oct. 22, 2009.  
 “Syntheses of Polyester/Poly(dimethylsiloxane)/Polyester Triblock Copolymers and their Rearrangement Under Water: Rearrangement of PDMS-containing Copolymers” authored by Lee and published in Composite Interfaces, (2006) 13 (2-3), 159-171.  
 “Asymmetric ABC-Triblock Copolymer Membranes Induce a Directed Insertion of Membrane Proteins” authored by Stoenescu et al. and published in Macromolecular Bioscience (2004) 4, 930-935.

\* cited by examiner

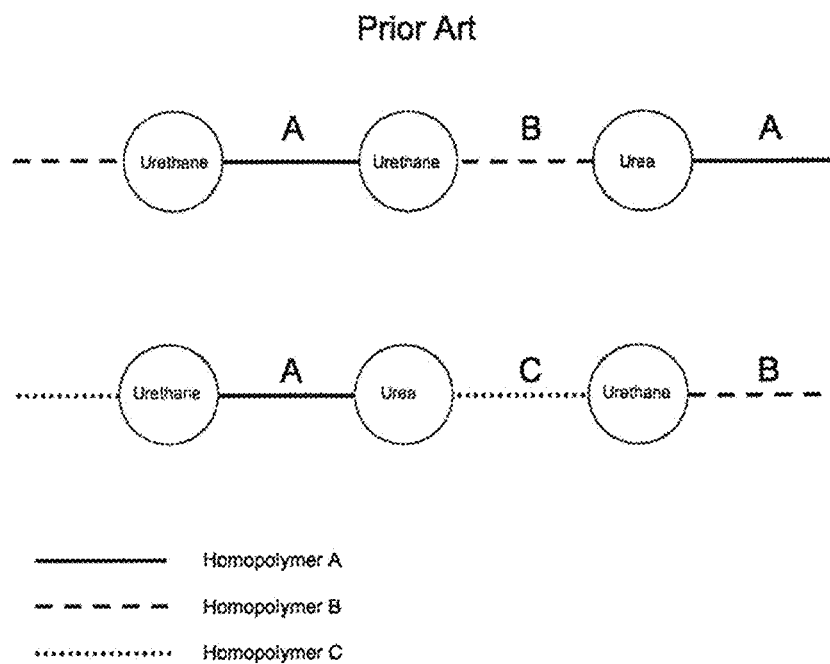


Figure 1

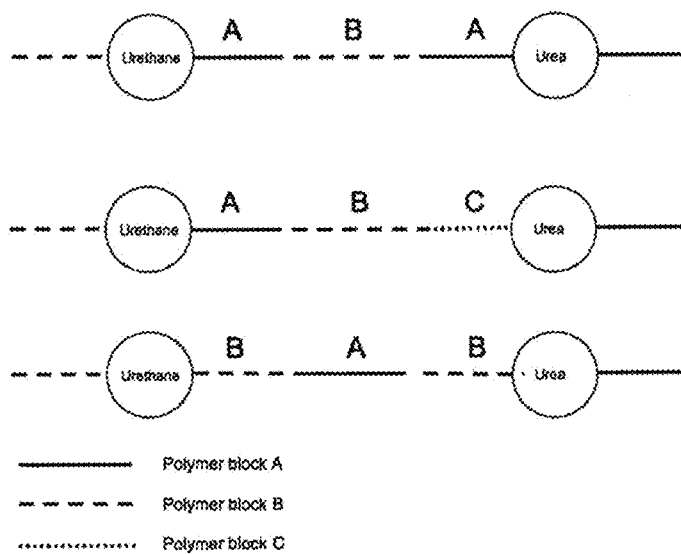


Figure 2

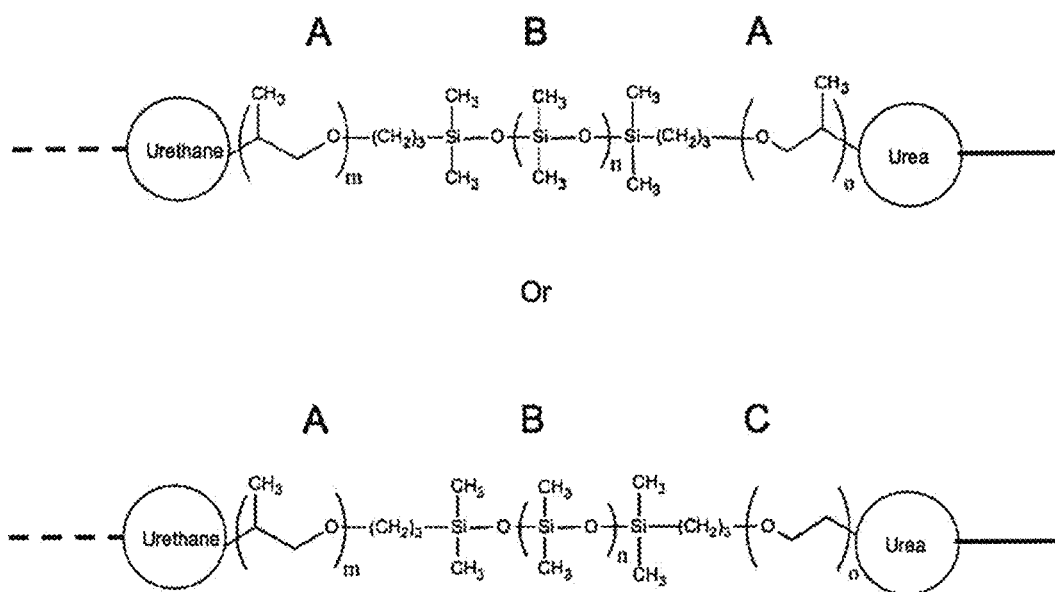


Figure 3

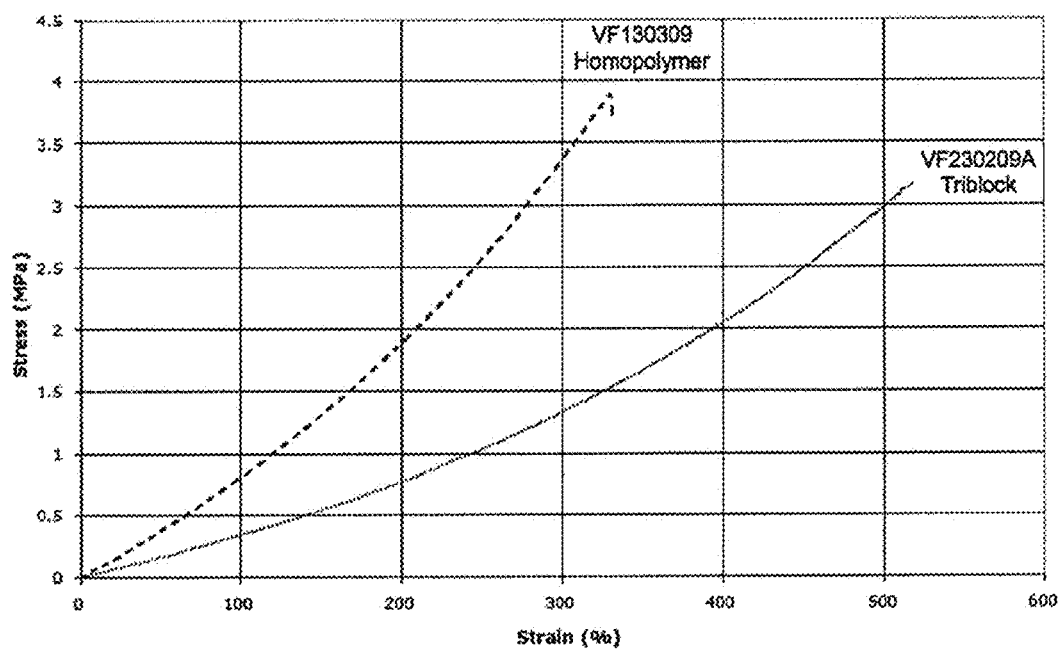


Figure 4

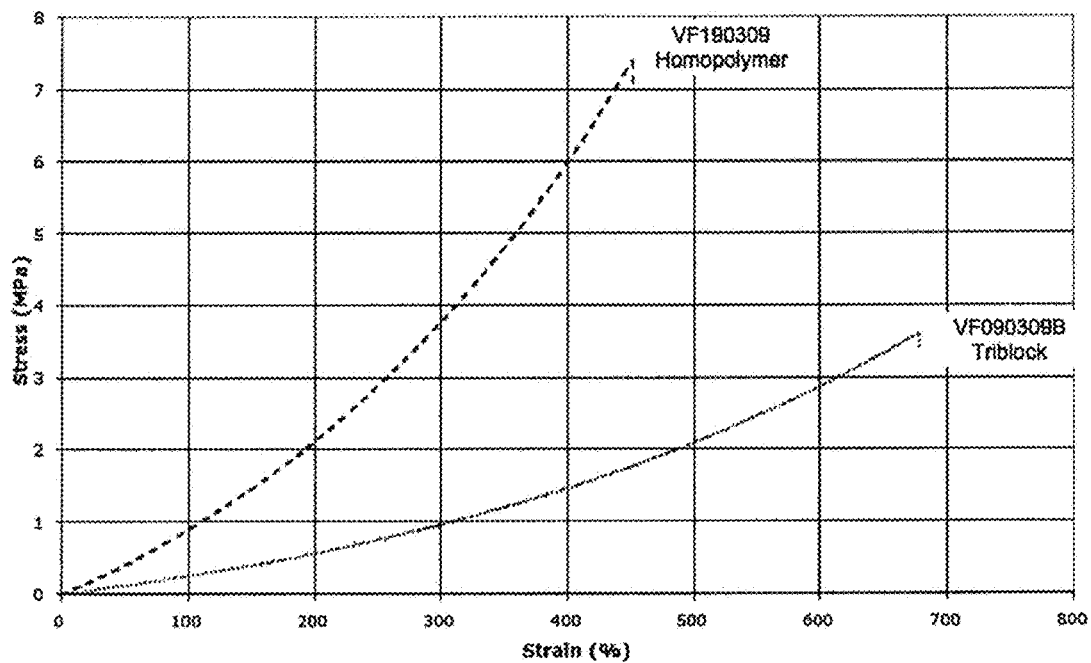
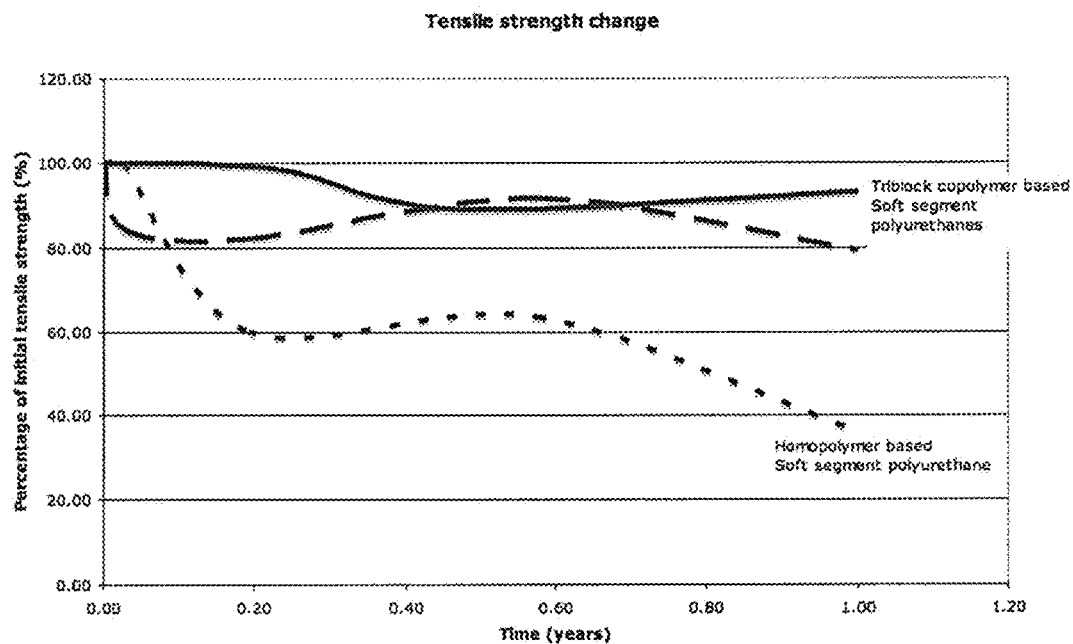


Figure 5

**Figure 6**

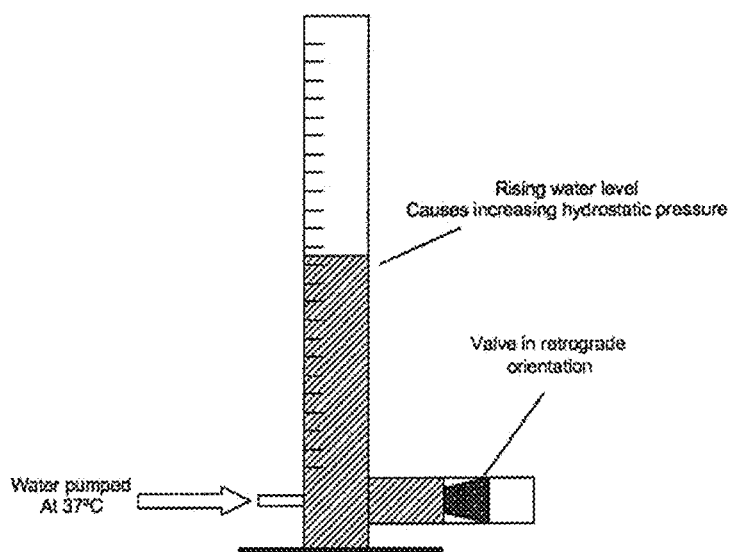
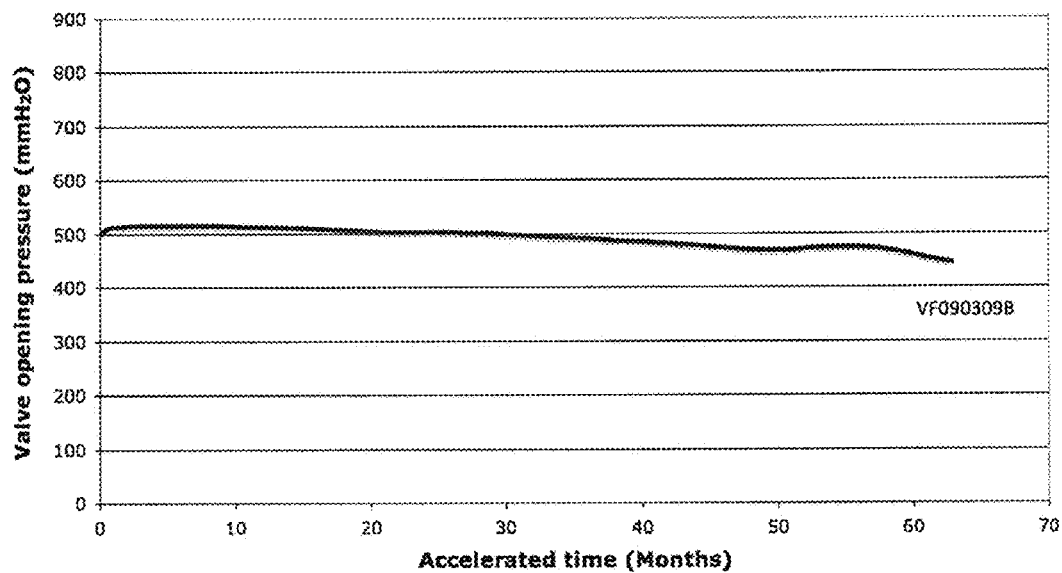
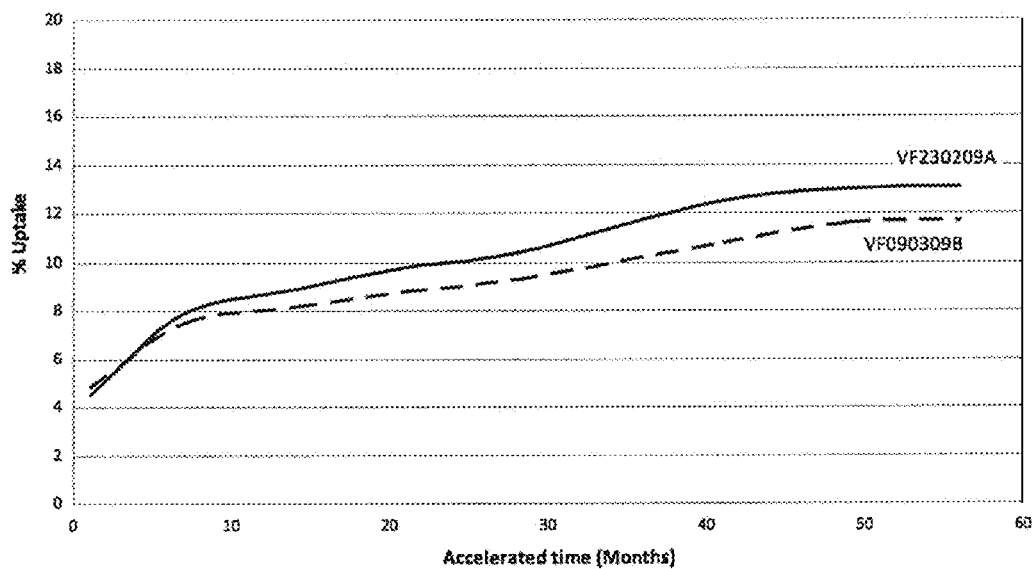


Figure 7

**Valve Function stability in Simulated Gastric Fluid****Figure 8A****Mass uptake of Simulated Gastric Fluid****Figure 8B**

1

## BIOMATERIAL

## CROSS-REFERENCE TO RELATED APPLICATIONS

The present application is a continuation of U.S. patent application Ser. No. 13/048,005, filed Mar. 15, 2011, the entire content of which is incorporated herein by reference and which is a continuation of U.S. patent application Ser. No. 12/488,047, filed Jun. 19, 2009, the entire content of which is incorporated herein by reference. The present application also claims the benefit of U.S. provisional patent application Nos. 61/074,400, filed Jun. 20, 2008, and 61/181,043, filed May 26, 2009, the entire contents of both of which are incorporated herein by reference.

## BACKGROUND OF THE INVENTION

Polyurethane and polyurea polymers are well known in the art and have been in use for decades. With a wide variety of potential chemical structures and properties these polymers have found applications in many diverse fields. In recent years polyurethanes have been extensively used in biomedical applications due to their accepted biocompatibility.

The structure of a polyurethane polymer can be generally described as a copolymer with a soft segment and a hard segment. The hard segment generally has stiffer bonds than the soft segment, which is reflected in a higher glass transition temperature ( $T_g$ ). The stiffness of the hard segment can be attributed to the presence of a urethane/urea group or oligomer. The molecular weight ratio of hard segment to soft segment has a critical impact on the mechanical properties of the final polymer as does the chemical nature of either segment.

Historically, in the preparation of polyurethane polymers, chemists have used polyethers as soft segments due to the mobility of their chains. Typical polyether polymers are polyethylene oxide (PEO), polypropylene oxide (PPO) or the higher homologues.

PEO and to a much lesser extent PPO can facilitate additional hydrogen bonding between segments thus yielding improved mechanical characteristics. Reduction in the ability of the soft segment to hydrogen bond with the hard segment has generally lead to poor tensile strengths.

Polyethers also impart significant hydrophilicity to polyurethanes but the effect decreases with higher polyether homologues. The propensity for these materials to undergo hydrolytic, oxidative and enzymatic degradation increases with hydrophilicity.

In more recent years alternative polymers have been used as soft segments to improve the biostability of polyurethanes but the mechanical properties of these have been limited.

The hard segment of a polyurethane polymer is the region rich in urethane or urea linkages formed from the reaction of diisocyanate molecules. These may be a single urethane or urea linkage or may be multiple repeat units covalently bound via urethane or urea bonds.

Diisocyanates can be divided into aromatic type and aliphatic type. The aromatic type is the preferred molecule. Aromatic diisocyanates yield bonds that have restricted rotation and thus low mobility due to their bulky nature. Such aromatic systems provide stiff chains to function as hard segments, which mechanically reinforce a polymer improving greatly the tensile properties of the polymer.

2

Aliphatic diisocyanates on the other hand typically form bonds of greater mobility thus resulting in hard segments which do not contribute greatly to the mechanical properties on the final polymer.

In recent years biostable polyurethanes have received a lot of attention and there are now several commercial products of this type that are designed for implantation in the body. These products tend to be solid elastomers of varying hardness.

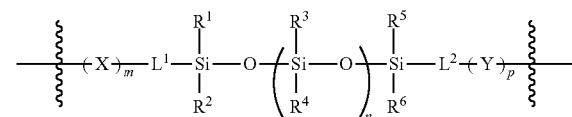
In order to achieve improvements in biostability varying proportions of the conventional and chemically labile polyether soft segments have been substituted with more robust molecules. Examples of improved soft segment molecules include polyolefins, polycarbonates and polysiloxanes.

However, incorporation of such alternative soft segments into polyurethane formulations, reduces the ability of the soft segment to form hydrogen and other intermolecular bonds with neighbouring chains. This limits the elongation and tensile properties of the final material. In addition, because many of the new biostable soft segments are hydrophobic they induce incompatibility with aqueous reagents. Because foam formation in polyurethane chemistry involves reaction with water (water blowing) such reactions are not reliable currently with hydrophobic soft segments.

In summary, there is an emerging trend towards more biostable commercial polyurethane materials utilising unconventional soft segments. However, all of the emerging materials are elastomers and no foams are available. In addition, because many of the newer soft segment materials do not hydrogen bond well they lack mechanical characteristics which are desirable for some applications.

## SUMMARY OF THE INVENTION

According to certain embodiments of the invention there is provided a triblock copolymer of formula I:



wherein the copolymers are chemically interspersed (bound) between urethane and/or urea linkages and wherein each of X, Y, m, n, p,  $L^1$ ,  $L^2$ ,  $R^1$ ,  $R^2$ ,  $R^3$ ,  $R^4$ ,  $R^5$ , and  $R^6$  is as defined and described herein.

In certain embodiments, the present invention provides a polyurethane/urea foam comprising a triblock copolymer of formula I as defined and described herein.

In some embodiments, the present invention provides a pre-formed soft segment for a polyurethane/urea foam wherein the soft segment is of formula I as defined and described herein.

## BRIEF DESCRIPTION OF THE DRAWINGS

FIG. 1 is an illustration of prior art polymers with urea and urethane linkages interspersed between homopolymer soft segments;

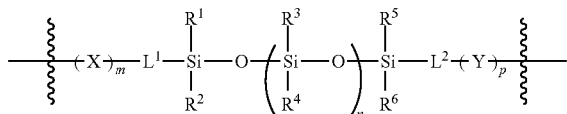
FIG. 2 is an illustration of a polyurethane/urea foam according to the invention with urea and urethane linkages interspersed between triblock copolymer soft segments;

FIG. 3 is an illustration of a siloxane and polypropylene oxide based triblock copolymer in different forms;

FIG. 8A and FIG. 8B depict results of accelerated stability of a valve prepared from a viscoelastic foam of the present invention.

## 1. General Description

Thus, in some embodiments, the present invention provides a multiblock copolymer that is biomimetic and hydrolytically stable in a gastric environment. Such multiblock copolymers are of formula I:



each R is independently hydrogen, an optionally substituted C<sub>1-20</sub> aliphatic group, or an optionally substituted group selected from phenyl, 8-10 membered bicyclic aryl, a 4-8 membered monocyclic saturated or partially unsaturated heterocyclic ring having 1-2 heteroatoms independently

each of m, n and p is independently 2 to 100; and each of L<sup>1</sup> and L<sup>2</sup> is independently a bivalent C<sub>1-20</sub> hydrocarbon chain wherein 1-4 methylene units of the hydrocarbon chain are optionally and independently replaced by —O—, —S—, —N(R)—, —C(O)—, —C(O)N(R)—, —N(R)C(O)—, —SO<sub>2</sub>—, —SO<sub>2</sub>N(R)—, —N(R)SO<sub>2</sub>—, —OC(O)—, —C(O)O—, or a bivalent cycloalkylene, arylene, heterocyclylene, or heteroarylene, provided that neither of L<sup>1</sup> nor L<sup>2</sup> comprises a urea or urethane moiety.

## 2. Definitions

The term “aliphatic” or “aliphatic group”, as used herein, denotes a hydrocarbon moiety that may be straight-chain (i.e., unbranched), branched, or cyclic (including fused, bridging, and spiro-fused polycyclic) and may be completely saturated or may contain one or more units of unsaturation, but which is not aromatic. Unless otherwise specified, aliphatic groups contain 1-20 carbon atoms. In some embodiments, aliphatic groups contain 1-10 carbon atoms. In other embodiments, aliphatic groups contain 1-8 carbon atoms. In still other embodiments, aliphatic groups contain 1-6 carbon atoms, and in yet other embodiments aliphatic groups contain 1-4 carbon atoms. Suitable aliphatic groups include, but are not limited

5

to, linear or branched, alkyl, alkenyl, and alkynyl groups, and hybrids thereof such as (cycloalkyl)alkyl, (cycloalkenyl)alkyl or (cycloalkyl)alkenyl.

The term "lower alkyl" refers to a  $C_{1-4}$  straight or branched alkyl group. Exemplary lower alkyl groups are methyl, ethyl, propyl, isopropyl, butyl, isobutyl, and tert-butyl.

The term "lower haloalkyl" refers to a  $C_{1-4}$  straight or branched alkyl group that is substituted with one or more halogen atoms.

The term "heteroatom" means one or more of oxygen, sulfur, nitrogen, phosphorus, or silicon (including, any oxidized form of nitrogen, sulfur, phosphorus, or silicon; the quaternized form of any basic nitrogen or; a substitutable nitrogen of a heterocyclic ring, for example N (as in 3,4-dihydro-2H-pyrrolyl), NH (as in pyrrolidinyl) or  $NR^+$  (as in N-substituted pyrrolidinyl)).

The term "unsaturated", as used herein, means that a moiety has one or more units of unsaturation.

As used herein, the term "bivalent  $C_{1-8}$  [or  $C_{1-6}$ ] saturated or unsaturated, straight or branched, hydrocarbon chain", refers to bivalent alkylene, alkenylene, and alkynylene chains that are straight or branched as defined herein.

The term "alkylene" refers to a bivalent alkyl group. An "alkylene chain" is a polymethylene group, i.e.,  $-(CH_2)_n-$ , wherein n is a positive integer, preferably from 1 to 6, from 1 to 4, from 1 to 3, from 1 to 2, or from 2 to 3. A substituted alkylene chain is a polymethylene group in which one or more methylene hydrogen atoms are replaced with a substituent. Suitable substituents include those described below for a substituted aliphatic group.

The term "alkenylene" refers to a bivalent alkenyl group. A substituted alkenylene chain is a polymethylene group containing at least one double bond in which one or more hydrogen atoms are replaced with a substituent. Suitable substituents include those described below for a substituted aliphatic group.

The term "halogen" means F, Cl, Br, or I.

The term "aryl" used alone or as part of a larger moiety as in "aralkyl", "aralkoxy", or "aryloxyalkyl", refers to monocyclic or bicyclic ring systems having a total of five to fourteen ring members, wherein at least one ring in the system is aromatic and wherein each ring in the system contains 3 to 7 ring members. The term "aryl" may be used interchangeably with the term "aryl ring".

As described herein, compounds of the invention may contain "optionally substituted" moieties. In general, the term "substituted", whether preceded by the term "optionally" or not, means that one or more hydrogens of the designated moiety are replaced with a suitable substituent. Unless otherwise indicated, an "optionally substituted" group may have a suitable substituent at each substitutable position of the group, and when more than one position in any given structure may be substituted with more than one substituent selected from a specified group, the substituent may be either the same or different at every position. Combinations of substituents envisioned by this invention are preferably those that result in the formation of stable or chemically feasible compounds. The term "stable", as used herein, refers to compounds that are not substantially altered when subjected to conditions to allow for their production, detection, and, in certain embodiments, their recovery, purification, and use for one or more of the purposes disclosed herein.

Suitable monovalent substituents on a substitutable carbon atom of an "optionally substituted" group are independently halogen;  $-(CH_2)_{0-4}R^o$ ;  $-(CH_2)_{0-4}OR^o$ ;  $-O-(CH_2)_{0-4}C(O)OR^o$ ;  $-(CH_2)_{0-4}CH(OR^o)_2$ ;  $-(CH_2)_{0-4}SR^o$ ;  $-(CH_2)_{0-4}Ph$ , which may be substituted with  $R^o$ ;  $-(CH_2)_{0-4}O(CH_2)_{0-1}$

6

Ph which may be substituted with  $R^o$ ;  $-\text{CH}=\text{CHPh}$ , which may be substituted with  $R^o$ ;  $-\text{NO}_2$ ;  $-\text{CN}$ ;  $-\text{N}_3$ ;  $-(CH_2)_{0-4}N(R^o)_2$ ;  $-(CH_2)_{0-4}N(R^o)C(O)R^o$ ;  $-N(R^o)C(S)R^o$ ;  $-(CH_2)_{0-4}N(R^o)C(O)NR^o$ ;  $-N(R^o)C(S)NR^o$ ;  $-(CH_2)_{0-4}N(R^o)C(O)OR^o$ ;  $-N(R^o)N(R^o)C(O)R^o$ ;  $-N(R^o)N(R^o)C(O)NR^o$ ;  $-N(R^o)N(R^o)C(O)OR^o$ ;  $-(CH_2)_{0-4}C(O)R^o$ ;  $-C(S)R^o$ ;  $-(CH_2)_{0-4}C(O)OR^o$ ;  $-(CH_2)_{0-4}C(O)SR^o$ ;  $-(CH_2)_{0-4}C(O)OSiR^o_3$ ;  $-(CH_2)_{0-4}OC(O)R^o$ ;  $-OC(O)(CH_2)_{0-4}SR$ ;  $SC(S)SR^o$ ;  $-(CH_2)_{0-4}SC(O)R^o$ ;  $-(CH_2)_{0-4}C(O)NR^o_2$ ;  $-C(S)NR^o_2$ ;  $-C(S)SR^o$ ;  $-SC(S)SR^o$ ;  $-(CH_2)_{0-4}OC(O)NR^o_2$ ;  $-C(O)N(OR^o)R^o$ ;  $-C(O)C(O)R^o$ ;  $-C(O)CH_2C(O)R^o$ ;  $-C(NOR^o)R^o$ ;  $-(CH_2)_{0-4}SSR^o$ ;  $-(CH_2)_{0-4}S(O)_2R^o$ ;  $-(CH_2)_{0-4}S(O)_2OR^o$ ;  $-(CH_2)_{0-4}OS(O)_2R^o$ ;  $-S(O)_2NR^o_2$ ;  $-(CH_2)_{0-4}S(O)R^o$ ;  $-N(R^o)S(O)_2NR^o_2$ ;  $-N(R^o)S(O)_2R^o$ ;  $-N(OR^o)R^o$ ;  $-C(NH)NR^o_2$ ;  $-P(O)_2R^o$ ;  $-P(O)R^o$ ;  $-OP(O)R^o_2$ ;  $-OP(O)(OR^o)_2$ ;  $SiR^o_3$ ;  $-(C_{1-4}$  straight or branched alkylene) $O-N(R^o)_2$ ; or  $-(C_{1-4}$  straight or branched alkylene) $C(O)O-N(R^o)_2$ , wherein each  $R^o$  may be substituted as defined below and is independently hydrogen,  $C_{1-6}$  aliphatic,  $-\text{CH}_2\text{Ph}$ ,  $-\text{O}(\text{CH}_2)_{0-1}\text{Ph}$ , or a 5-6-membered saturated, partially unsaturated, or aryl ring having 0-4 heteroatoms independently selected from nitrogen, oxygen, or sulfur, or, notwithstanding the definition above, two independent occurrences of  $R^o$ , taken together with their intervening atom(s), form a 3-12-membered saturated, partially unsaturated, or aryl mono- or bicyclic ring having 0-4 heteroatoms independently selected from nitrogen, oxygen, or sulfur, which may be substituted as defined below.

Suitable monovalent substituents on  $R^o$  (or the ring formed by taking two independent occurrences of  $R^o$  together with their intervening atoms), are independently halogen,  $-(CH_2)_{0-2}R$ ,  $-(\text{halo}R)$ ,  $-(CH_2)_{0-2}OH$ ,  $-(CH_2)_{0-2}OR$ ,  $-(CH_2)_{0-2}CH(OR)_2$ ,  $-O(\text{halo}R)$ ,  $-\text{CN}$ ,  $-\text{N}_3$ ,  $-(CH_2)_{0-2}C(O)R$ ,  $-(CH_2)_{0-2}C(O)OH$ ,  $-(CH_2)_{0-2}C(O)OR$ ,  $-(CH_2)_{0-2}SR$ ,  $-(CH_2)_{0-2}SH$ ,  $-(CH_2)_{0-2}NH_2$ ,  $-(CH_2)_{0-2}NHR$ ,  $-(CH_2)_{0-2}NR_2$ ,  $-\text{NO}_2$ ,  $-\text{SiR}_3$ ,  $-\text{OSiR}_3$ ,  $-C(O)SR$ ,  $-(C_{1-4}$  straight or branched alkylene) $C(O)OR$ , or  $-\text{SSR}$ , wherein each R is unsubstituted or where preceded by "halo" is substituted only with one or more halogens, and is independently selected from  $C_{1-4}$  aliphatic,  $-\text{CH}_2\text{Ph}$ ,  $-\text{O}(\text{CH}_2)_{0-1}\text{Ph}$ , or a 5-6-membered saturated, partially unsaturated, or aryl ring having 0-4 heteroatoms independently selected from nitrogen, oxygen, or sulfur. Suitable divalent substituents on a saturated carbon atom of  $R^o$  include  $=O$  and  $=S$ .

Suitable divalent substituents on a saturated carbon atom of an "optionally substituted" group include the following:  $=O$ ,  $=S$ ,  $=\text{NNR}^*_2$ ,  $=\text{NNHC}(O)R^*$ ,  $=\text{NNHC}(O)OR^*$ ,  $=\text{NNHS}(O)_2R^*$ ,  $=\text{NR}^*$ ,  $=\text{NOR}^*$ ,  $-\text{O}(\text{C}(R^*_2))_{2-3}O-$ , or  $-\text{S}(\text{C}(R^*_2))_{2-3}S-$ , wherein each independent occurrence of  $R^*$  is selected from hydrogen,  $C_{1-6}$  aliphatic which may be substituted as defined below, or an unsubstituted 5-6-membered saturated, partially unsaturated, or aryl ring having 0-4 heteroatoms independently selected from nitrogen, oxygen, or sulfur. Suitable divalent substituents that are bound to vicinal substitutable carbons of an "optionally substituted" group include:  $-\text{O}(\text{C}(R^*_2))_{2-3}O$ , wherein each independent occurrence of  $R^*$  is selected from hydrogen,  $C_{1-6}$  aliphatic which may be substituted as defined below, or an unsubstituted 5-6-membered saturated, partially unsaturated, or aryl ring having 0-4 heteroatoms independently selected from nitrogen, oxygen, or sulfur.

Suitable substituents on the aliphatic group of  $R^*$  include halogen,  $-R$ ,  $-(\text{halo}R)$ ,  $-\text{OH}$ ,  $-\text{OR}$ ,  $-\text{O}(\text{halo}R)$ ,  $-\text{CN}$ ,  $-C(O)OH$ ,  $-C(O)OR$ ,  $-\text{NH}_2$ ,  $-\text{NHR}$ ,  $-\text{NR}_2$ , or  $-\text{NO}_2$ , wherein each R is unsubstituted or where preceded

by "halo" is substituted only with one or more halogens, and is independently  $C_{1-4}$  aliphatic,  $-\text{CH}_2\text{Ph}$ ,  $-\text{O}(\text{CH}_2)_{0-1}\text{Ph}$ , or a 5-6-membered saturated, partially unsaturated, or aryl ring having 0-4 heteroatoms independently selected from nitrogen, oxygen, or sulfur.

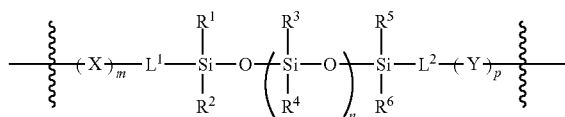
Suitable substituents on a substitutable nitrogen of an "optionally substituted" group include  $-\text{R}^+$ ,  $-\text{NR}^+_{2-}$ ,  $-\text{C}(\text{O})\text{R}^+$ ,  $-\text{C}(\text{O})\text{OR}^+$ ,  $-\text{C}(\text{O})\text{C}(\text{O})\text{R}^+$ ,  $-\text{C}(\text{O})\text{CH}_2\text{C}(\text{O})\text{R}^+$ ,  $-\text{S}(\text{O})_2\text{R}^+$ ,  $-\text{S}(\text{O})_2\text{NR}^+_{2-}$ ,  $-\text{C}(\text{S})\text{NR}^+_{2-}$ ,  $-\text{C}(\text{NH})\text{NR}^+_{2-}$ , or  $-\text{N}(\text{R}^+)\text{S}(\text{O})_2\text{R}^+$ ; wherein each  $\text{R}^+$  is independently hydrogen,  $C_1$  aliphatic which may be substituted as defined below, unsubstituted  $-\text{OPh}$ , or an unsubstituted 5-6-membered saturated, partially unsaturated, or aryl ring having 0-4 heteroatoms independently selected from nitrogen, oxygen, or sulfur, or, notwithstanding the definition above, two independent occurrences of  $\text{R}^+$ , taken together with their intervening atom(s) form an unsubstituted 3-12-membered saturated, partially unsaturated, or aryl mono- or bicyclic ring having 0-4 heteroatoms independently selected from nitrogen, oxygen, or sulfur.

Suitable substituents on the aliphatic group of  $\text{R}^+$  are independently halogen,  $-\text{R}$ .,  $-(\text{haloR})$ .,  $-\text{OH}$ .,  $-\text{OR}$ .,  $-\text{O}(\text{haloR})$ .,  $-\text{CN}$ .,  $-\text{C}(\text{O})\text{OH}$ .,  $-\text{C}(\text{O})\text{OR}$ .,  $-\text{NH}_2$ .,  $-\text{NHR}$ .,  $-\text{NR}_2$ ., or  $-\text{NO}_2$ ., wherein each  $\text{R}$  is unsubstituted or where preceded by "halo" is substituted only with one or more halogens, and is independently  $C_{1-4}$  aliphatic,  $-\text{CH}_2\text{Ph}$ ,  $-\text{O}(\text{CH}_2)_{0-1}\text{Ph}$ , or a 5-6-membered saturated, partially unsaturated, or aryl ring having 0-4 heteroatoms independently selected from nitrogen, oxygen, or sulfur.

### 3. Description of Exemplary Embodiments

#### A. Multiblock Copolymers

As described generally above, one embodiment of the present invention provides a triblock copolymer of formula I:



wherein the copolymers are chemically interspersed (bound) between urethane and/or urea linkages (i.e., at the bond designated with  $\xi$ ) and wherein each of X, Y, m, n, p,  $\text{L}^1$ ,  $\text{L}^2$ ,  $\text{R}^1$ ,  $\text{R}^2$ ,  $\text{R}^3$ ,  $\text{R}^4$ ,  $\text{R}^5$ , and  $\text{R}^6$  is as defined and described herein.

As defined generally above, the each of X and Y groups of formula I is independently a polymer or co-polymer chain formed from one or more of a polyether, a polyester, a polycarbonate, and a fluoropolymer.

Examples of polymer or co-polymer chains represented by X and/or Y include: poly(ethylene oxide), poly(difluoromethyl ethylene oxide), poly(trifluoromethyl ethylene oxide), poly(propylene oxide), poly(difluoromethyl propylene oxide), poly(propylene oxide), poly(trifluoromethyl propylene oxide), poly(butylene oxide), poly(tetramethylene ether glycol), poly(tetrahydrofuran), poly(oxymethylene), poly(ether ketone), poly(etherether ketone) and copolymers thereof, poly(dimethylsiloxane), poly(diethylsiloxane) and higher alkyl siloxanes, poly(methyl phenyl siloxane), poly(diphenyl siloxane), poly(methyl di-fluoroethyl siloxane), poly(methyl tri-fluoroethyl siloxane), poly(phenyl di-fluoro-

ethyl siloxane), poly(phenyl tri-fluoroethyl siloxane) and copolymers thereof, poly(ethylene terephthalate) (PET), poly(ethylene terephthalate ionomer) (PETI), poly(ethylene naphthalate) (PEN), poly(methylene naphthalate) (PTN), poly(butylene terephthalate) (PBT), poly(butylene naphthalate) (PBN), polycarbonate.

In certain embodiments, the present invention provides a pre-formed soft segment for a polyurethane/urea foam

In some embodiments X is a polyether and Y is a polyether. More specifically in one case X and Y are both poly(propylene oxide).

In certain embodiments, m and p are each independently between 2 and 50 and n is between 2 and 20. In some embodiments, m and p are each independently between 2 and 30 and n is between 2 and 20.

As defined generally above, each of  $\text{R}^1$ ,  $\text{R}^2$ ,  $\text{R}^3$ ,  $\text{R}^4$ ,  $\text{R}^5$  and  $\text{R}^6$  is independently selected from one or more of R, OR,  $-\text{CO}_2\text{R}$ , a fluorinated hydrocarbon, a polyether, a polyester or a fluoropolymer. In some embodiments, one or more of  $\text{R}^1$ ,  $\text{R}^2$ ,  $\text{R}^3$ ,  $\text{R}^4$ ,  $\text{R}^5$  and  $\text{R}^6$  is  $-\text{CO}_2\text{R}$ . In some embodiments, one or more of  $\text{R}^1$ ,  $\text{R}^2$ ,  $\text{R}^3$ ,  $\text{R}^4$ ,  $\text{R}^5$  and  $\text{R}^6$  is  $-\text{CO}_2\text{R}$  wherein each R is independently an optionally substituted  $C_{1-6}$  aliphatic group. In certain embodiments, one or more of  $\text{R}^1$ ,  $\text{R}^2$ ,  $\text{R}^3$ ,  $\text{R}^4$ ,  $\text{R}^5$  and  $\text{R}^6$  is  $-\text{CO}_2\text{R}$  wherein each R is independently an unsubstituted  $C_{1-6}$  alkyl group. Exemplary such groups include methanoic or ethanoic acid as well as methacrylic acid and other acrylic acids.

In certain embodiments, one or more of  $\text{R}^1$ ,  $\text{R}^2$ ,  $\text{R}^3$ ,  $\text{R}^4$ ,  $\text{R}^5$  and  $\text{R}^6$  is independently R. In some embodiments, one or more of  $\text{R}^1$ ,  $\text{R}^2$ ,  $\text{R}^3$ ,  $\text{R}^4$ ,  $\text{R}^5$  and  $\text{R}^6$  is an optionally substituted  $C_{1-6}$  aliphatic group. In certain embodiments, one or more of  $\text{R}^1$ ,  $\text{R}^2$ ,  $\text{R}^3$ ,  $\text{R}^4$ ,  $\text{R}^5$  and  $\text{R}^6$  is an optionally substituted  $C_{1-6}$  alkyl. In other embodiments, one or more of  $\text{R}^1$ ,  $\text{R}^2$ ,  $\text{R}^3$ ,  $\text{R}^4$ ,  $\text{R}^5$  and  $\text{R}^6$  is an optionally substituted group selected from phenyl, 8-10 membered bicyclic aryl, a 4-8 membered monocyclic saturated or partially unsaturated heterocyclic ring having 1-2 heteroatoms independently selected from nitrogen, oxygen, or sulphur, or 5-6 membered monocyclic or 8-10 membered bicyclic heteroaryl group having 1-4 heteroatoms independently selected from nitrogen, oxygen, or sulphur. Exemplary such  $\text{R}^1$ ,  $\text{R}^2$ ,  $\text{R}^3$ ,  $\text{R}^4$ ,  $\text{R}^5$  and  $\text{R}^6$  groups include methyl, ethyl, propyl, isopropyl, cyclopropyl, butyl, isobutyl, cyclobutyl, phenyl, pyridyl, morpholinyl, pyrrolidinyl, imidazolyl, and cyclohexyl.

In certain embodiments, one or more of  $\text{R}^1$ ,  $\text{R}^2$ ,  $\text{R}^3$ ,  $\text{R}^4$ ,  $\text{R}^5$  and  $\text{R}^6$  is independently OR. In some embodiments, one or more of  $\text{R}^1$ ,  $\text{R}^2$ ,  $\text{R}^3$ ,  $\text{R}^4$ ,  $\text{R}^5$  and  $\text{R}^6$  is  $-\text{OR}$  wherein R is an optionally substituted  $C_{1-6}$  aliphatic group. In certain embodiments, one or more of  $\text{R}^1$ ,  $\text{R}^2$ ,  $\text{R}^3$ ,  $\text{R}^4$ ,  $\text{R}^5$  and  $\text{R}^6$  is  $-\text{OR}$  wherein R is  $C_{1-6}$  alkyl. In other embodiments, one or more of  $\text{R}^1$ ,  $\text{R}^2$ ,  $\text{R}^3$ ,  $\text{R}^4$ ,  $\text{R}^5$  and  $\text{R}^6$  is  $-\text{OR}$  wherein R is an optionally substituted group selected from phenyl, 8-10 membered bicyclic aryl, a 4-8 membered monocyclic saturated or partially unsaturated heterocyclic ring having 1-2 heteroatoms independently selected from nitrogen, oxygen, or sulphur, or 5-6 membered monocyclic or 8-10 membered bicyclic heteroaryl group having 1-4 heteroatoms independently selected from nitrogen, oxygen, or sulphur. Exemplary such  $\text{R}^1$ ,  $\text{R}^2$ ,  $\text{R}^3$ ,  $\text{R}^4$ ,  $\text{R}^5$  and  $\text{R}^6$  groups include  $-\text{O}$ methyl,  $-\text{O}$ ethyl,  $-\text{O}$ propyl,  $-\text{O}$ isopropyl,  $-\text{O}$ cyclopropyl,  $-\text{O}$ butyl,  $-\text{O}$ isobutyl,  $-\text{O}$ cyclobutyl,  $-\text{O}$ phenyl,  $-\text{O}$ pyridyl,  $-\text{O}$ morpholinyl,  $-\text{O}$ pyrrolidinyl,  $-\text{O}$ imidazolyl, and  $-\text{O}$ cyclohexyl.

In certain embodiments, one or more of  $\text{R}^1$ ,  $\text{R}^2$ ,  $\text{R}^3$ ,  $\text{R}^4$ ,  $\text{R}^5$  and  $\text{R}^6$  is independently R wherein each R is a  $C_{1-6}$  aliphatic group substituted with one or more halogens. In some embodiments, each R is  $C_{1-6}$  aliphatic substituted with one,

two, or three halogens. In other embodiments, each R is a perfluorinated C<sub>1-6</sub> aliphatic group. Examples of fluorinated hydrocarbons represented by R<sup>1</sup>, R<sup>2</sup>, R<sup>3</sup>, R<sup>4</sup>, R<sup>5</sup> and R<sup>6</sup> include mono-, di-, tri-, or perfluorinated methyl, ethyl, propyl, butyl, or phenyl. In some embodiments, each of R<sup>1</sup>, R<sup>2</sup>, R<sup>3</sup>, R<sup>4</sup>, R<sup>5</sup> and R<sup>6</sup> is trifluoromethyl, trifluoroethyl, or trifluoropropyl.

In certain embodiments, one or more of R<sup>1</sup>, R<sup>2</sup>, R<sup>3</sup>, R<sup>4</sup>, R<sup>5</sup> and R<sup>6</sup> is independently a polyether. Examples of polyethers represented by R<sup>1</sup>, R<sup>2</sup>, R<sup>3</sup>, R<sup>4</sup>, R<sup>5</sup> and R<sup>6</sup> include poly(ethylene oxide), poly(difluoromethyl ethylene oxide), poly(trifluoromethyl ethylene oxide), poly(propylene oxide), poly(difluoromethyl propylene oxide), poly(propylene oxide), poly(trifluoromethyl propylene oxide), poly(butylene oxide), poly(tetramethylene ether glycol), poly(tetrahydrofuran), poly(oxyethylene), poly(ether ketone), poly(ether ether ketone) and copolymers thereof.

In certain embodiments, one or more of R<sup>1</sup>, R<sup>2</sup>, R<sup>3</sup>, R<sup>4</sup>, R<sup>5</sup> and R<sup>6</sup> is independently a polyester. Examples of polyesters represented by R<sup>1</sup>, R<sup>2</sup>, R<sup>3</sup>, R<sup>4</sup>, R<sup>5</sup> and R<sup>6</sup> include poly(ethylene terephthalate) (PET), poly(ethylene terephthalate ionomer) (PETI), poly(ethylene naphthalate) (PEN), poly(methylene naphthalate) (PTN), poly(butylene terephthalate) (PBT), poly(butylene naphthalate) (PBN), polycarbonate.

In certain embodiments, one or more of R<sup>1</sup>, R<sup>2</sup>, R<sup>3</sup>, R<sup>4</sup>, R<sup>5</sup> and R<sup>6</sup> is independently a fluoropolymer. Examples of fluoropolymers represented by R<sup>1</sup>, R<sup>2</sup>, R<sup>3</sup>, R<sup>4</sup>, R<sup>5</sup> and R<sup>6</sup> include poly(tetrafluoroethylene), poly(methyl di-fluoroethyl siloxane), poly(methyl tri-fluoroethyl siloxane), poly(phenyl di-fluoroethyl siloxane).

In some embodiments, R<sup>1</sup>, R<sup>2</sup>, R<sup>3</sup>, R<sup>4</sup>, R<sup>5</sup> and R<sup>6</sup> is independently hydrogen, hydroxyl, carboxylic acids such as methanoic or ethanoic acid as well as methacrylic acid and other acrylic acids. Alkyl or aryl hydrocarbons such as methyl, ethyl, propyl, butyl, phenyl and ethers thereof. Fluorinated hydrocarbons such as mono-, di-, tri-, or perfluorinated methyl, ethyl, propyl, butyl, phenyl. Polyether such as Poly(ethylene oxide), poly(difluoromethyl ethylene oxide), poly(trifluoromethyl ethylene oxide), poly(propylene oxide), poly(difluoromethyl propylene oxide), poly(propylene oxide), poly(trifluoromethyl propylene oxide), poly(butylene oxide), poly(tetramethylene ether glycol), poly(tetrahydrofuran), poly(oxyethylene), poly(ether ketone), poly(ether ether ketone) and copolymers thereof. Polyesters such as Poly(ethylene terephthalate) (PET), poly(ethylene terephthalate ionomer) (PETI), poly(ethylene naphthalate) (PEN), poly(methylene naphthalate) (PTN), Poly(Butylene Terephthalate) (PBT), poly(butylene naphthalate) (PBN), polycarbonate and fluoropolymer such as Poly(tetrafluoroethylene), poly(methyl di-fluoroethyl siloxane), poly(methyl tri-fluoroethyl siloxane), poly(phenyl di-fluoroethyl siloxane).

In some embodiments, m and p are between 2 and 50 and n is between 2 and 20. In certain embodiments, m and o are between 2 and 30 and n is between 2 and 20.

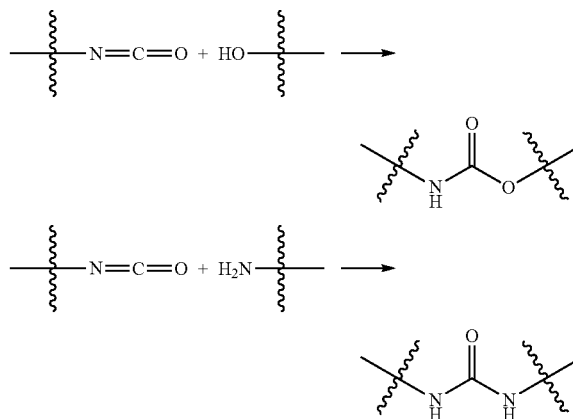
As defined generally above, each of L<sup>1</sup> and L<sup>2</sup> is independently a bivalent C<sub>1-20</sub> hydrocarbon chain wherein 1-4 methylene units of the hydrocarbon chain are optionally and independently replaced by —O—, —S—, —N(R)—, —C(O)—, —C(O)N(R)—, —N(R)C(O)—, —SO<sub>2</sub>—, —SO<sub>2</sub>N(R)—, —N(R)SO<sub>2</sub>—, —OC(O)—, —C(O)O—, or a bivalent cycloalkylene, arylene, heterocyclene, or heteroarylene, provided that neither of L<sup>1</sup> nor L<sup>2</sup> comprises a urea or urethane moiety. In some embodiments, each of L<sup>1</sup> and L<sup>2</sup> is independently a bivalent C<sub>1-20</sub> alkylene chain. In certain embodiments, each of L<sup>1</sup> and L<sup>2</sup> is independently a bivalent C<sub>1-10</sub> alkylene chain. In certain

embodiments, each of L<sup>1</sup> and L<sup>2</sup> is independently a bivalent C<sub>1-4</sub> alkylene chain. Exemplary such L<sup>1</sup> and L<sup>2</sup> groups include methylene, ethylene, propylene, butylene or higher bivalent alkanes.

In some embodiments, each of L<sup>1</sup> and L<sup>2</sup> is independently a bivalent C<sub>1-20</sub> alkylene chain wherein one methylene unit of the chain is replaced by —O—. In some embodiments, each of L<sup>1</sup> and L<sup>2</sup> is independently a bivalent C<sub>1-10</sub> alkylene chain wherein one methylene unit of the chain is replaced by —O—. In some embodiments, each of L<sup>1</sup> and L<sup>2</sup> is independently a bivalent C<sub>1-6</sub> alkylene chain wherein one methylene unit of the chain is replaced by —O—. In some embodiments, each of L<sup>1</sup> and L<sup>2</sup> is independently a bivalent C<sub>1-4</sub> alkylene chain wherein one methylene unit of the chain is replaced by —O—. Exemplary such L<sup>1</sup> and L<sup>2</sup> groups include —OCH<sub>2</sub>—, —OCH<sub>2</sub>CH<sub>2</sub>—, —OCH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>—, —OCH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>—, or higher bivalent alkylene ethers.

In some embodiments, each of L<sup>1</sup> and L<sup>2</sup> is independently a bivalent C<sub>1-20</sub> alkylene chain wherein at least one methylene unit of the chain is replaced by —O— and at least one methylene unit of the chain is replaced by a bivalent arylene. In some embodiments, each of L<sup>1</sup> and L<sup>2</sup> is independently a bivalent C<sub>1-10</sub> alkylene chain wherein at least one methylene unit of the chain is replaced by —O— and at least one methylene unit of the chain is replaced by a bivalent arylene. In some embodiments, each of L<sup>1</sup> and L<sup>2</sup> is independently a bivalent C<sub>1-6</sub> alkylene chain wherein at least one methylene unit of the chain is replaced by —O— and at least one methylene unit of the chain is replaced by a bivalent arylene. In some embodiments, each of L<sup>1</sup> and L<sup>2</sup> is independently a bivalent C<sub>1-4</sub> alkylene chain wherein at least one methylene unit of the chain is replaced by —O— and at least one methylene unit of the chain is replaced by a bivalent arylene. Exemplary such L<sup>1</sup> and L<sup>2</sup> groups include —OCH<sub>2</sub>-phenylene-, —OCH<sub>2</sub>CH<sub>2</sub>-phenylene-, —OCH<sub>2</sub>CH<sub>2</sub>-phenylene-CH<sub>2</sub>—, —OCH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>-phenylene-, and the like.

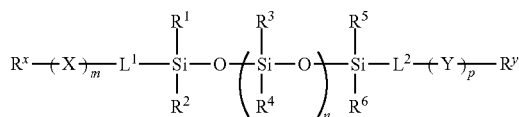
One of ordinary skill in the art would understand that a polyurethane results from the reaction of a diisocyanate and a hydroxyl group. Similarly, a polyurea results from the reaction of a diisocyanate and an amine. Each of these reactions is depicted below.



Thus, it is readily apparent that provided compounds of formula I can be functionalized with end groups suitable for forming urethane and/or urea linkages. In certain embodi

## 11

ments, the present invention provides a compound of formula II:



wherein:

each of  $\text{R}^x$  and  $\text{R}^y$  is independently  $-\text{OH}$ ,  $-\text{NH}_2$ , a protected hydroxyl or a protected amine;

each of  $\text{X}$  and  $\text{Y}$  is independently a polymer or co-polymer chain formed from one or more of a polyether, a polyester, a polycarbonate, and a fluoropolymer;

each of  $\text{R}^1$ ,  $\text{R}^2$ ,  $\text{R}^3$ ,  $\text{R}^4$ ,  $\text{R}^5$  and  $\text{R}^6$  is independently selected from one or more of  $\text{R}$ ,  $\text{OR}$ ,  $-\text{CO}_2\text{R}$ , a fluorinated hydrocarbon, a polyether, a polyester or a fluoropolymer;

each  $\text{R}$  is independently hydrogen, an optionally substituted  $\text{C}_{1-20}$  aliphatic group, or an optionally substituted group selected from phenyl, 8-10 membered bicyclic aryl, a 4-8 membered monocyclic saturated or partially unsaturated heterocyclic ring having 1-2 heteroatoms independently selected from nitrogen, oxygen, or sulphur, or 5-6 membered monocyclic or 8-10 membered bicyclic heteroaryl group having 1-4 heteroatoms independently selected from nitrogen, oxygen, or sulfur;

each of  $m$ ,  $n$  and  $p$  is independently 2 to 100; and

each of  $\text{L}^1$  and  $\text{L}^2$  is independently a bivalent  $\text{C}_{1-20}$  hydrocarbon chain wherein 1-4 methylene units of the hydrocarbon chain are optionally and independently replaced by  $-\text{O}-$ ,  $-\text{S}-$ ,  $-\text{N}(\text{R})-$ ,  $-\text{C}(\text{O})-$ ,  $-\text{C}(\text{O})\text{N}(\text{R})-$ ,  $-\text{N}(\text{R})\text{C}(\text{O})-$ ,  $-\text{SO}_2-$ ,  $-\text{SO}_2\text{N}(\text{R})-$ ,  $-\text{N}(\text{R})\text{SO}_2-$ ,  $-\text{OC}(\text{O})-$ ,  $-\text{C}(\text{O})\text{O}-$ , or a bivalent cycloalkylene, arylene, heterocyclene, or heteroarylene, provided that neither of  $\text{L}^1$  nor  $\text{L}^2$  comprises a urea or urethane moiety.

In some embodiments, each of  $\text{X}$ ,  $\text{Y}$ ,  $m$ ,  $n$ ,  $p$ ,  $\text{L}^1$ ,  $\text{L}^2$ ,  $\text{R}^1$ ,  $\text{R}^2$ ,  $\text{R}^3$ ,  $\text{R}^4$ ,  $\text{R}^5$ , and  $\text{R}^6$  is as defined and described herein.

As defined generally above, each of  $\text{R}^x$  and  $\text{R}^y$  is independently  $-\text{OH}$ ,  $-\text{NH}_2$ , a protected hydroxyl or a protected amine. In some embodiments, both of  $\text{R}^x$  and  $\text{R}^y$  are  $-\text{OH}$ . In other embodiments, both of  $\text{R}^x$  and  $\text{R}^y$  are  $-\text{NH}_2$ . In some embodiments one of  $\text{R}^x$  and  $\text{R}^y$  is  $-\text{OH}$  and the other is  $-\text{NH}_2$ .

In some embodiments, each of  $\text{R}^x$  and  $\text{R}^y$  is independently a protected hydroxyl or a protected amine. Such protected hydroxyl and protected amine groups are well known to one of skill in the art and include those described in detail in *Protecting Groups in Organic Synthesis*, T. W. Greene and P. G. M. Wuts, 3rd edition, John Wiley & Sons, 1999, the entirety of which is incorporated herein by reference. Exemplary protected amines include methyl carbamate, ethyl carbamate, 9-fluorenylmethyl carbamate (Fmoc), 9-(2-sulfo)fluorenylmethyl carbamate, 9-(2,7-dibromo)fluorenylmethyl carbamate, 2,7-di-*t*-butyl-[9-(10,10-dioxo-10,10,10-tetrahydrothioxanthyl)]methyl carbamate (DBD-Tmoc), 4-methoxyphenacyl carbamate (Phenoc), 2,2,2-trichloroethyl carbamate (Troc), 2-trimethylsilyl ethyl carbamate (Teoc), 2-phenylethyl carbamate (hZ), 1-(1-adamantyl)-1-methylethyl carbamate (Adpoc), 1,1-dimethyl-2-haloethyl carbamate, 1,1-dimethyl-2,2-dibromoethyl carbamate (DB-t-BOC), 1,1-dimethyl-2,2,2-trichloro ethyl carbamate (TCBOC), 1-methyl-1-(4-biphenyl)ethyl carbamate (Bpoc), 1-(3,5-di-*t*-butylphenyl)-1-methylethyl carbamate (t-Bumeoc), 2-(2'- and 4'-pyridyl)ethyl carbamate

## 12

(Pyoc), 2-(*N,N*-dicyclohexylcarboxamido)ethyl carbamate, *t*-butyl carbamate (BOC), 1-adamantyl carbamate (Adoc), vinyl carbamate (Voc), allyl carbamate (Alloc), 1-isopropylallyl carbamate (Ipaoc), cinnamyl carbamate (Coc), 4-nitrocinnamyl carbamate (Noc), 8-quinolyl carbamate, *N*-hydroxypiperidinyl carbamate, alkyldithio carbamate, benzyl carbamate (Cbz), *p*-methoxybenzyl carbamate (Moz), *p*-nitrobenzyl carbamate, *p*-bromobenzyl carbamate, *p*-chlorobenzyl carbamate, 2,4-dichlorobenzyl carbamate, 4-methylsulfinylbenzyl carbamate (MsZ), 9-anthrylmethyl carbamate, diphenylmethyl carbamate, 2-methylthioethyl carbamate, 2-methylsulfonyl ethyl carbamate, 2-(*p*-toluenesulfonyl)ethyl carbamate, [2-(1,3-dithianyl)]methyl carbamate (Dmoc), 4-methylthiophenyl carbamate (Mtpc), 2,4-dimethylthiophenyl carbamate (Bmpc), 2-phosphonio ethyl carbamate (Peoc), 2-triphenylphosphonioisopropyl carbamate (Ppoc), 1,1-dimethyl-2-cyanoethyl carbamate, *m*-chloro-*p*-acyloxybenzyl carbamate, *p*-(dihydroxyboryl)benzyl carbamate, 5-benzisoxazolylmethyl carbamate, 2-(trifluoromethyl)-6-chromonylmethyl carbamate (Troc), *m*-nitrophenyl carbamate, 3,5-dimethoxybenzyl carbamate, *o*-nitrobenzyl carbamate, 3,4-dimethoxy-6-nitrobenzyl carbamate, phenyl(*o*-nitrophenyl)methyl carbamate, phenothiazinyl-(10)-carbonyl derivative, *N'*-*p*-toluenesulfonylamino carbonyl derivative, *N'*-phenylaminothiocarbonyl derivative, *t*-amyl carbamate, *S*-benzyl thiocarbamate, *p*-cyanobenzyl carbamate, cyclobutyl carbamate, cyclohexyl carbamate, cyclopentyl carbamate, cyclopropylmethyl carbamate, *p*-decyloxybenzyl carbamate, 2,2-dimethoxycarbonylvinyl carbamate, *o*-(*N,N*-dimethylcarboxamido)benzyl carbamate, 1,1-dimethyl-3-(*N,N*-dimethylcarboxamido)propyl carbamate, 1,1-dimethylpropynyl carbamate, di(2-pyridyl)methyl carbamate, 2-furanylmethyl carbamate, 2-iodoethyl carbamate, isoborynl carbamate, isobutyl carbamate, isonicotinyl carbamate, *p*-(*p'*-methoxyphenylazo)benzyl carbamate, 1-methylcyclobutyl carbamate, 1-methylcyclohexyl carbamate, 1-methyl-1-cyclopropylmethyl carbamate, 1-methyl-1-(3,5-dimethoxyphenyl)ethyl carbamate, 1-methyl-1-(*p*-phenylazophenyl)ethyl carbamate, 1-methyl-1-phenylethyl carbamate, 1-methyl-1-(4-pyridyl)ethyl carbamate, phenyl carbamate, *p*-(phenylazo)benzyl carbamate, 2,4,6-tri-*t*-butylphenyl carbamate, 4-(trimethylammonium)benzyl carbamate, 2,4,6-trimethylbenzyl carbamate, formamide, acetamide, chloroacetamide, trichloroacetamide, trifluoroacetamide, phenylacetamide, 3-phenylpropanamide, picolinamide, 3-pyridylcarboxamide, *N*-benzoylphenylalanine derivative, benzamide, *p*-phenylbenzamide, *o*-nitrophenylacetamide, *o*-nitrophenoxycetamide, acetoacetamide, (*N'*-dithiobenzyloxycarbonylamino)acetamide, 3-(*p*-hydroxyphenyl)propanamide, 3-(*o*-nitrophenyl)propanamide, 2-methyl-2-(*o*-nitrophenoxy)propanamide, 2-methyl-2-(*o*-phenylazophenoxy)propanamide, 4-chlorobutanamide, 3-methyl-3-nitrobutanamide, *o*-nitrocinnamide, *N*-acetylmethionine derivative, *o*-nitrobenzamide, *o*-(benzoyloxymethyl)benzamide, 4,5-diphenyl-3-oxazolin-2-one, *N*-phthalimide, *N*-dithiasuccinimide (Dts), *N*-2,3-diphenylmaleimide, *N*-2,5-dimethylpyrrole, *N*-1,1,4,4-tetramethyldisilylazacyclopentane adduct (STABASE), 5-substituted 1,3-dimethyl-1,3,5-triazacyclohexan-2-one, 5-substituted 1,3-dibenzyl-1,3,5-triazacyclohexan-2-one, 1-substituted 3,5-dinitro-4-pyridone, *N*-methylamine, *N*-allylamine, *N*-[2-(trimethylsilyl)ethoxy]methylamine (SEM), *N*-3-acetoxypropylamine, *N*-(1-isopropyl-4-nitro-2-oxo-3-pyrrool-3-yl)amine, quaternary ammonium salts, *N*-benzylamine, *N*-di(4-methoxyphenyl)methylamine, *N*-5-dibenzo-suberyllamine, *N*-triphenylmethylamine (Tr), *N*-[(4-methoxyphenyl)diphenylmethyl]amine (MMTr), *N*-9-

## 13

phenylfluorenylamine (PhF), N-2,7-dichloro-9-fluorenylmethyleneamine, N-ferrocenylmethylamino (Fcm), N-2-picolylamino N'-oxide, N-1,1-dimethylthiomethyleneamine, N-benzylidene amine, N-p-methoxybenzylidene amine, N-diphenylmethyleneamine, N-[(2-pyridyl)mesityl] methyleneamine, N-(N',N'-dimethylaminomethylene) amine, N,N'-isopropylidenediamine, N-p-nitrobenzylideneamine, N-salicylideneamine, N-5-chloro salicylideneamine, N-(5-chloro-2-hydroxyphenyl)phenylmethyleneamine, N-cyclohexylideneamine, N-(5,5-dimethyl-3-oxo-1-cyclohexenyl)amine, N-borane derivative, N-diphenylborinic acid derivative, N-[phenyl(pentacarbonylchromium- or tungsten) carbonyl]amine, N-copper chelate, N-zinc chelate, N-nitroamine, N-nitrosoamine, amine N-oxide, diphenylphosphinamide (Dpp), dimethylthiophosphinamide (Mpt), diphenylthiophosphinamide (Ppt), dialkyl phosphoramidates, dibenzyl phosphoramidate, diphenyl phosphoramidate, benzenesulfenamide, o-nitrobenzenesulfenamide (Nps), 2,4-dinitrobenzenesulfenamide, pentachlorobenzene-sulfenamide, 2-nitro-4-methoxybenzenesulfenamide, triphenylmethylsulfenamide, 3-nitropyridinesulfenamide (Npys), p-toluenesulfonamide (Ts), benzenesulfonamide, 2,3,6-trimethyl-4-methoxybenzenesulfonamide (Mtr), 2,4,6-trimethoxybenzenesulfonamide (Mtb), 2,6-dimethyl-4-methoxybenzene sulfonamide (Pme), 2,3,5,6-tetramethyl-4-methoxybenzenesulfonamide (Mte), 4-methoxybenzenesulfonamide (Mbs), 2,4,6-trimethylbenzenesulfonamide (Mts), 2,6-dimethoxy-4-methylbenzenesulfonamide (iMds), 2,2,5,7,8-pentamethylchroman-6-sulfonamide (Pmc), methanesulfonamide (Ms),  $\beta$ -trimethylsilyl ethanesulfonamide (SES), 9-anthracenesulfonamide, 4-(4',8'-dimethoxynaphthylmethyl)benzenesulfonamide (DNMBS), benzylsulfonamide, trifluoromethylsulfonamide, and phenacylsulfonamide.

Exemplary hydroxyl protecting groups include methyl, methoxymethyl (MOM), methylthiomethyl (MTM), t-butylthiomethyl, (phenyldimethylsilyl)methoxymethyl (SMOM), benzyloxymethyl (BOM), p-methoxybenzyloxymethyl (PMBM), (4-methoxyphenoxy)methyl (p-AOM), guaiacolmethyl (GUM), t-butoxymethyl, 4-pentenylloxymethyl (POM), siloxymethyl, 2-methoxyethoxymethyl (MEM), 2,2,2-trichloroethoxymethyl, bis(2-chloroethoxy)methyl, 2-(trimethylsilyl)ethoxymethyl (SEMOR), tetrahydropyranyl (THP), 3-bromotetrahydropyranyl, tetrahydrothiopyranyl, 1-methoxycyclohexyl, 4-methoxytetrahydropyranyl (MTHP), 4-methoxytetrahydrothiopyranyl, 4-methoxytetrahydrothiopyranyl S,S-dioxide, 1-[(2-chloro-4-methyl)phenyl]-4-methoxypiperidin-4-yl (CTMP), 1,4-dioxan-2-yl, tetrahydrofuranyl, tetrahydrothiofuranyl, 2,3,3a, 4,5,6,7,7a-octahydro-7,8,8-trimethyl-4,7-methanobenzofuran-2-yl, 1-ethoxyethyl, 1-(2-chloroethoxy)ethyl, 1-methyl-1-methoxyethyl, 1-methyl-1-benzyloxyethyl, 1-methyl-1-benzyloxy-2-fluoroethyl, 2,2,2-trichloroethyl, 2-trimethylsilyl ethyl, 2-(phenylselenyl)ethyl, t-butyl, allyl, p-chlorophenyl, p-methoxyphenyl, 2,4-dinitrophenyl, benzyl, p-methoxybenzyl, 3,4-dimethoxybenzyl, o-nitrobenzyl, p-nitrobenzyl, p-halobenzyl, 2,6-dichlorobenzyl, p-cyanobenzyl, p-phenylbenzyl, 2-picolyl, 4-picolyl, 3-methyl-2-picolyl N-oxido, diphenylmethyl, p,p'-dinitrobenzhydryl, 5-dibenzosuberyl, triphenylmethyl,  $\alpha$ -naphthylidiphenylmethyl, p-methoxyphenyldiphenylmethyl, di(p-methoxyphenyl)phenylmethyl, tri(p-methoxyphenyl)methyl, 4-(4'-bromophenacyloxyphenyl)diphenylmethyl, 4,4',4"-tris(4,5-dichlorophthalimidophenyl)methyl, 4,4',4"-tris(levulinoyloxyphenyl)methyl, 4,4',4"-tris(benzoyloxyphenyl)methyl, 3-(imidazol-1-yl)bis(4',4"-dimethoxyphenyl)methyl, 1,1-bis(4-methoxyphenyl)-1'-pyrenylmethyl,

## 14

9-anthryl, 9-(9-phenyl)xanthenyl, 9-(9-phenyl-10-oxo)anthryl, 1,3-benzodithiolan-2-yl, benzoisothiazolyl S,S-dioxido, trimethylsilyl (TMS), triethylsilyl (TES), triisopropylsilyl (TIPS), dimethylisopropylsilyl (IPDMS), diethylisopropylsilyl (DEIPS), dimethylhexylsilyl, t-butyl dimethylsilyl (TB-DMS), t-butyl diphenylsilyl (TBDPS), tribenzylsilyl, tri-p-xylylsilyl, triphenylsilyl, diphenylmethylsilyl (DPMS), t-butylmethoxyphenylsilyl (TBMPS), formate, benzoylformate, acetate, chloroacetate, dichloroacetate, trichloroacetate, trifluoroacetate, methoxyacetate, triphenylmethoxyacetate, phenoxyacetate, p-chlorophenoxyacetate, 3-phenylpropionate, 4-oxopentanoate (levulinate), 4,4-(ethylenedithio)pentanoate (levulinoyldithioacetal), pivaloate, adamantate, crotonate, 4-methoxycrotonate, benzoate, p-phenylbenzoate, 2,4,6-trimethylbenzoate (mesitoate), alkyl methyl carbonate, 9-fluorenylmethyl carbonate (Fmoc), alkyl ethyl carbonate, alkyl 2,2,2-trichloroethyl carbonate (Troc), 2-(trimethylsilyl)ethyl carbonate (TMSEC), 2-(phenylsulfonyl)ethyl carbonate (Psec), 2-(triphenylphosphonio)ethyl carbonate (Peoc), alkyl isobutyl carbonate, alkyl vinyl carbonate alkyl allyl carbonate, alkyl p-nitrophenyl carbonate, alkyl benzyl carbonate, alkyl p-methoxybenzyl carbonate, alkyl 3,4-dimethoxybenzyl carbonate, alkyl o-nitrobenzyl carbonate, alkyl p-nitrobenzyl carbonate, alkyl S-benzyl thiocarbonate, 4-ethoxy-1-naphthyl carbonate, methyl dithiocarbonate, 2-iodobenzoate, 4-azidobutyrate, 4-nitro-4-methylpentanoate, o-(dibromomethyl)benzoate, 2-formylbenzenesulfonate, 2-(methylthiomethoxy)ethyl, 4-(methylthiomethoxy)butyrate, 2-(methylthiomethoxymethyl)benzoate, 2,6-dichloro-4-methylphenoxyacetate, 2,6-dichloro-4-(1,1,3,3-tetramethylbutyl)phenoxyacetate, 2,4-bis(1,1-dimethylpropyl)phenoxyacetate, chlorodiphenylacetate, isobutyrate, mono succinoate, (E)-2-methyl-2-butenate, o-(methoxycarbonyl)benzoate,  $\alpha$ -naphthoate, nitrate, alkyl N,N,N',N'-tetramethylphosphorodiamidate, alkyl N-phenylcarbamate, borate, dimethylphosphinothioyl, alkyl 2,4-dinitrophenylsulfenate, sulfate, methanesulfonate (mesylate), benzylsulfonate, and tosylate (Ts). For protecting 1,2- or 1,3-diols, the protecting groups include methylene acetal, ethylidene acetal, 1-t-butylethylidene ketal, 1-phenylethylidene ketal, (4-methoxyphenyl)ethylidene acetal, 2,2,2-trichloroethylidene acetal, acetone, cyclopentylidene ketal, cyclohexylidene ketal, cycloheptylidene ketal, benzylidene acetal, p-methoxybenzylidene acetal, 2,4-dimethoxybenzylidene ketal, 3,4-dimethoxybenzylidene acetal, 2-nitrobenzylidene acetal, methoxymethylene acetal, ethoxymethylene acetal, dimethoxymethylene ortho ester, 1-methoxyethylidene ortho ester, 1-ethoxyethylidene ortho ester, 1,2-dimethoxyethylidene ortho ester,  $\alpha$ -methoxybenzylidene ortho ester, 1-(N,N-dimethylamino)ethylidene derivative,  $\alpha$ -(N,N'-dimethylamino)benzylidene derivative, 2-oxacyclopentylidene ortho ester, di-t-butylsilylene group (DTBS), 1,3-(1,1,3,3-tetraisopropylidisiloxanylidene) derivative (TIPDS), tetra-t-butoxydisiloxane-1,3-diylidene derivative (TBDS), cyclic carbonates, cyclic boronates, ethyl boronate, and phenyl boronate.

One of ordinary skill in the art will appreciate that the choice of hydroxyl and amine protecting groups can be such that these groups are removed at the same time (e.g., when both protecting groups are acid labile or base labile). Alternatively, such groups can be removed in a step-wise fashion (e.g., when one protecting group is removed first by one set of removal conditions and the other protecting group is removed second by a different set of removal conditions). Such methods are readily understood by one of ordinary skill in the art.

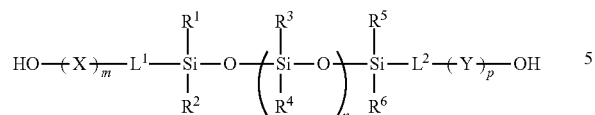
In certain embodiments, the present invention provides a compound of any of formulae II-a, II-b, II-c, and II-d:

15

16

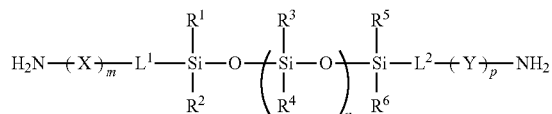
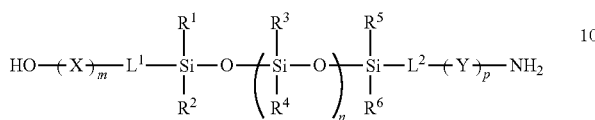
-continued

II-a

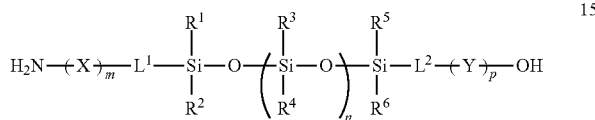


II-d

II-b

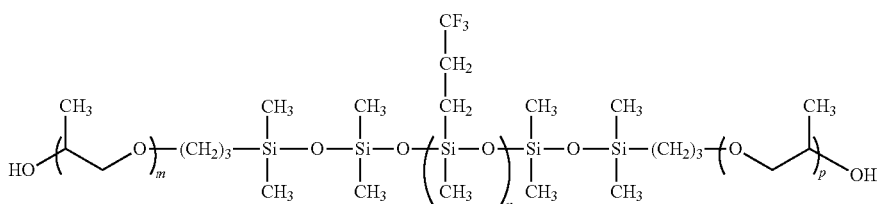
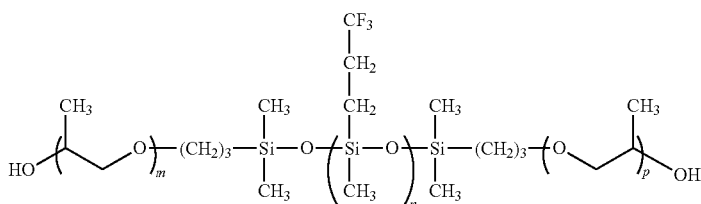
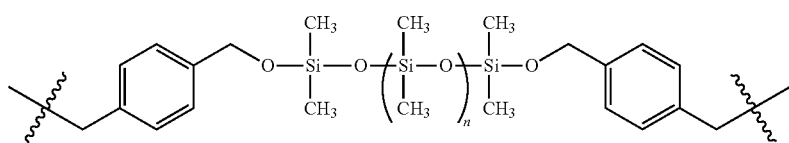
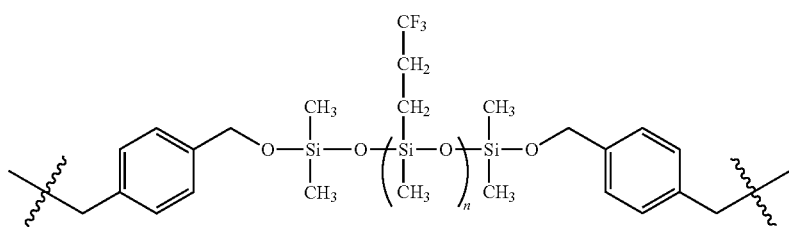
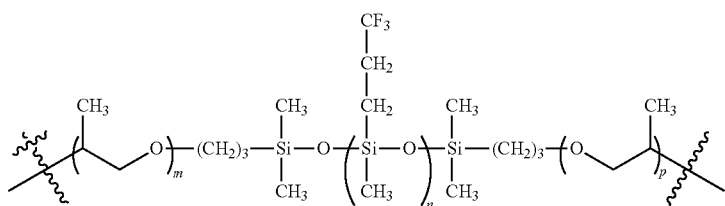
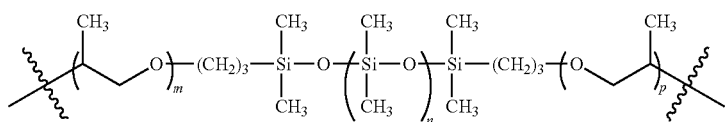


II-c



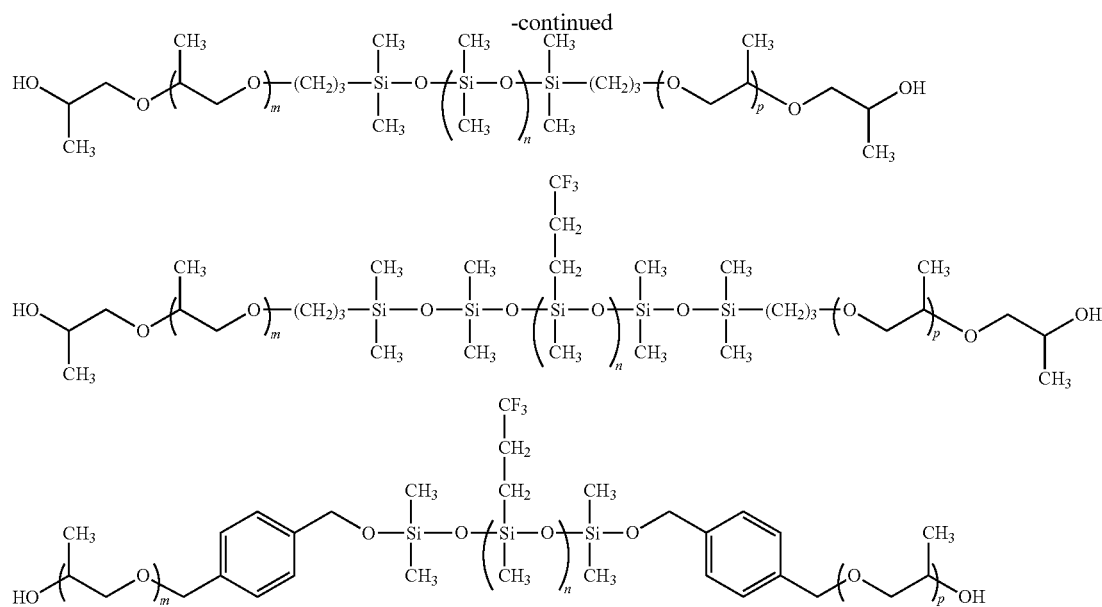
wherein each of X, Y, m, n, p, L<sup>1</sup>, L<sup>2</sup>, R<sup>1</sup>, R<sup>2</sup>, R<sup>3</sup>, R<sup>4</sup>, R<sup>5</sup>, and R<sup>6</sup> is as defined and described herein.

Exemplary triblock copolymers of the present invention are set forth below:



17

18

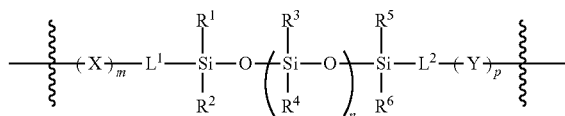


25

wherein each of m, n, and p is as defined and described herein.

In some embodiments, the present invention provides a polymer foam, comprising:

(a) one or more triblock copolymers of formula I:



wherein each of X, Y, m, n, p, L<sup>1</sup>, L<sup>2</sup>, R<sup>1</sup>, R<sup>2</sup>, R<sup>3</sup>, R<sup>4</sup>, R<sup>5</sup>, and R<sup>6</sup> is as defined and described herein; and

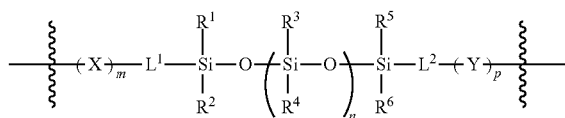
(b) wherein the copolymers are chemically interspersed (bound) between urethane and/or urea linkages (i.e., at

the bond designated with  $\xi$ ).

The invention further provides a pre-formed soft segment of the formula I as defined above. In some embodiments, the present invention provides a polyurethane/urea foam comprising a soft segment triblock copolymer of formula I.

In some embodiments, the present invention provides a viscoelastic biostable water blown foam, comprising:

(a) one or more triblock copolymers of formula I:



wherein each of X, Y, m, n, p, L<sup>1</sup>, L<sup>2</sup>, R<sup>1</sup>, R<sup>2</sup>, R<sup>3</sup>, R<sup>4</sup>, R<sup>5</sup>, and R<sup>6</sup> is as defined and described herein; and

(b) wherein the copolymers are chemically interspersed (bound) between urethane and/or urea linkages (i.e., at

the bond designated with  $\xi$ ).

It has been surprisingly found that polyurethanes and/or polyureas comprising a triblock copolymer of the present invention are stable to gastric fluid. Such polyurethanes and polyureas prepared using triblock copolymers of the present invention are viscoelastic and stable to gastric fluid. In some embodiments, a provided viscoelastic material is a foam.

In certain embodiments, a provided biostable foam is stable to gastric fluid. In some embodiments, a provided biostable foam is stable to gastric fluid for at least one year. In some embodiments, a provided biostable foam is stable to gastric fluid for at least 3 months, for at least 4 months, for at least 5 months, for at least 6 months, for at least 7 months, for at least 8 months, for at least 9 months, for at least 10 months, for at least 11 months, or for at least one year. Methods for determining stability of a provided biostable foam are known in the art utilizing simulated gastric fluid and include those described in detail in the Exemplification, *infra*.

In some embodiments, a provided viscoelastic foam, comprising a triblock copolymer of the present invention, is characterized in that the foam takes up less than about 30% by weight of water at equilibrium. In certain embodiments, a provided viscoelastic foam takes up less than about 5%, less than about 10%, less than about 15%, less than about 20%, less than about 25%, or less than about 30% by weight of water at equilibrium. One of ordinary skill in the art will appreciate that such chemical stability (i.e., in gastric fluid and therefore at very low pH) and hydrophobicity (i.e., water uptake of less than about 30% by weight) are characteristics that differ dramatically from known siloxane polymers that are utilized in, e.g., the manufacture of contact lenses. For example, siloxane polymer that are utilized in, e.g., the manufacture of contact lenses require a water uptake of 50-120%.

As described above, the present invention provides a viscoelastic foam comprising a triblock copolymer of the present invention. It was surprisingly found that a provided foam has a high elongation capacity and the ability to recover very slowly following elongation. Indeed, it was found that a provided viscoelastic foam has an elongation capacity of about 200-1200%. In some embodiments, a provided viscoelastic foam has an elongation capacity of about 500%.

19

In some embodiments, a provided viscoelastic foam has a tensile strength of about 0.1 to about 1.0 MPa. In certain embodiments, a provided viscoelastic foam has a tensile strength of about 0.25 to about 0.5 MPa.

In some embodiments, a provided viscoelastic foam has a Young's Modulus of about 0.1 to about 0.6 MPa. In certain embodiments, a provided viscoelastic foam has a Young's Modulus of about 0.1 to about 0.5 MPa.

One of ordinary skill in the art will appreciate that, depending upon the physical characteristics required for a particular use of a provided foam, a foam of varying densities can be prepared. For example, a valve having a thinner wall would require a foam having a higher density than a similar valve having a thicker wall in order to result in each valve having a similar physical characteristic (e.g., tensile strength, and the like). Thus, in certain embodiments, a provided viscoelastic foam has a density of 0.1 to 1.5 g/cm<sup>3</sup>. In certain embodiments, a provided viscoelastic foam has a density of 0.3 to 1.2 g/cm<sup>3</sup>. In certain embodiments, a provided viscoelastic foam has a density of 0.8 to 0.9 g/cm<sup>3</sup>. In some embodiments, a provided viscoelastic foam has a density of 0.5 to 0.6 g/cm<sup>3</sup>.

In certain embodiments, the present invention provides polyether-siloxane and polyether-fluorosiloxane polyurethane materials with a greatly reduced number of weak-links as illustrated by FIG. 2 and FIG. 3. This was achieved by performing the soft segment prior to the polyurethane reaction. In the examples below a triblock copolymer based on polydimethyl siloxane and polypropylene oxide was used but it will be appreciated that other triblock copolymers such as those formed from polysiloxanes and poly(ethylene oxide), poly(difluoromethyl ethylene oxide), poly(trifluoromethyl ethylene oxide), poly(propylene oxide), poly(difluoromethyl propylene oxide), poly(propylene oxide), poly(trifluoromethyl propylene oxide), poly(butylene oxide), poly(tetramethylene ether glycol), poly(tetrahydrofuran), poly(oxymethylene), poly(ether ketone), poly(etherether ketone) and copolymers thereof, poly(dimethylsiloxane), poly(diethylsiloxane) and higher alkyl siloxanes, poly(methyl phenyl siloxane), poly(diphenyl siloxane), poly(methyl di-fluoroethyl

20

the constituent homopolymers as soft segments that the mechanical characteristics and hydrolytic stability of the resulting material is substantially improved.

In some embodiments, the present invention provides a foam comprising a copolymer of the present invention. Such foams offer specific advantages over solid elastomers, especially for gastrointestinal device applications. These advantages include enhanced biostability in the gastric environment, compressibility, viscoelasticity and high 'surface area to volume ratio'. The foam formulations of the invention can mimic mechanical characteristics of the native gastrointestinal tissue.

A biostable water blown foam was prepared from heterogeneous reagents.

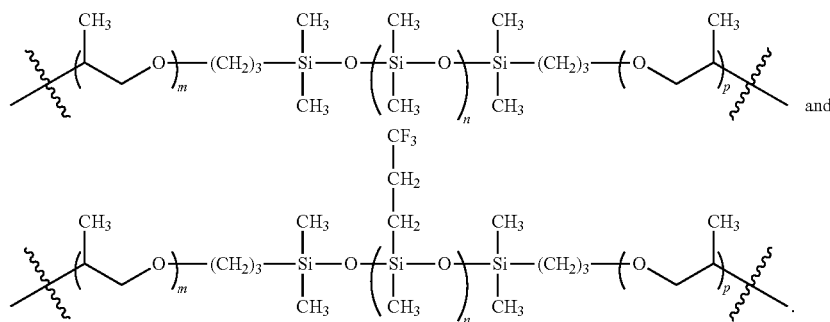
The prior art describes polyurethane foams that are prepared by the sequential reaction of polymer chains to one another resulting in a high molecular weight solid material. In all cases the polymeric precursors described in the art are linked together by urethane/urea linkages as illustrated in FIG. 1. However, each urethane/urea linkage is a possible site for degradation.

In the invention we have prepared a biostable polyurethane/urea foam with much fewer 'weak links' by using copolymer precursors as shown in FIG. 2.

Polyurethane reactions have historically been carried out in a single phase due to ease of processing. However, we have made novel materials by combining physically heterogeneous reaction pre-cursors together to form a stable two-phase dispersion ('water-in-oil') which was then reacted to form a foam.

#### EXEMPLIFICATION

In two specific examples X and Y are both polyethers namely poly(propylene oxide) (PPO). These were formulated into copolymers with poly(dimethylsiloxane) (PDMS) and poly(trifluoropropyl methylsiloxane) respectively in varying ratios as described by the following formulae:

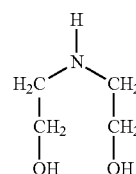


siloxane), poly(methyl tri-fluoroethyl siloxane), poly(phenyl di-fluoroethyl siloxane), poly(phenyl tri-fluoroethyl siloxane) and copolymers thereof, poly(ethylene terephthalate) (PET), poly(ethylene terephthalate ionomer) (PETI), poly(ethylene naphthalate) (PEN), poly(methylene naphthalate) (PTN), poly(butylene terephthalate) (PBT), poly(butylene naphthalate) (PBN) and polycarbonate could be used.

Referring to FIG. 2, copolymers of the form ABA, ABC and BAB were produced from homopolymers of polysiloxane and polypropylene oxide which were covalently linked using bonds less labile than urethane/urea. The molecular weight and chemical characteristics of such homopolymers were tailored to achieve a pre-soft-segment with the appropriate balance of hydrophilicity/hydrophobicity. Without wishing to be bound by any particular theory, it is believed that by using a non-urethane linked tri-block copolymer instead of

The formulations contained a number of other components including:

Branching Agent—DEOA

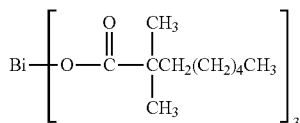


Diethanolamine (DEOA) is used as a branching agent although it is sometimes known as a crosslinking agent. The

## 21

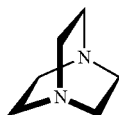
molecular weight of DEOA is 105.14 g/mol. The effect of the DEOA is to influence softness and elasticity of the end polymer.

Gelling Catalyst—Bismuth Neodecanoate (BICAT)



Bismuth neodecanoate is supplied as BiCat 8108M from Shepherd. It has a molecular weight of 722.75 g/mol. This catalyst is used to facilitate the complete reaction between isocyanate and hydroxyl or amine functional groups.

Blowing Catalyst—DABCO 33-lv



DABCO is a common blowing catalyst for reaction between NCO and H<sub>2</sub>O. It has a molecular weight of 112.17 g/mol. This catalyst has the effect, in combination with H<sub>2</sub>O, of manipulating the foam rise characteristics.

### Example 1

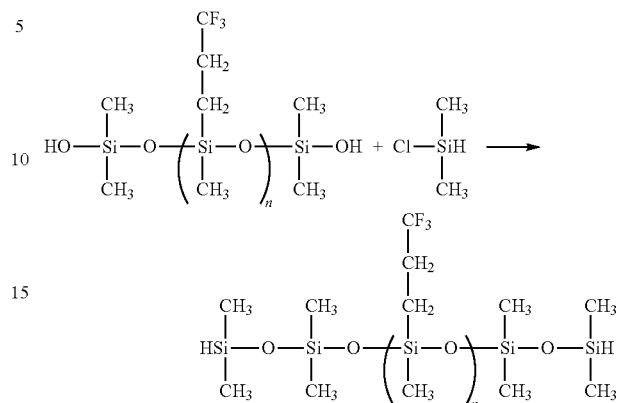
### Synthesis of Aliphatic Linked Fluorosiloxane Based Triblock Copolymer Pre-Soft-Segment

This is a 2 step process. In the first step silanol terminated poly(trifluoropropyl methyl siloxane) is converted into its dihydride derivative. In the next step, this dihydride derivative is reacted with the allyl terminated poly(propylene glycol).

## 22

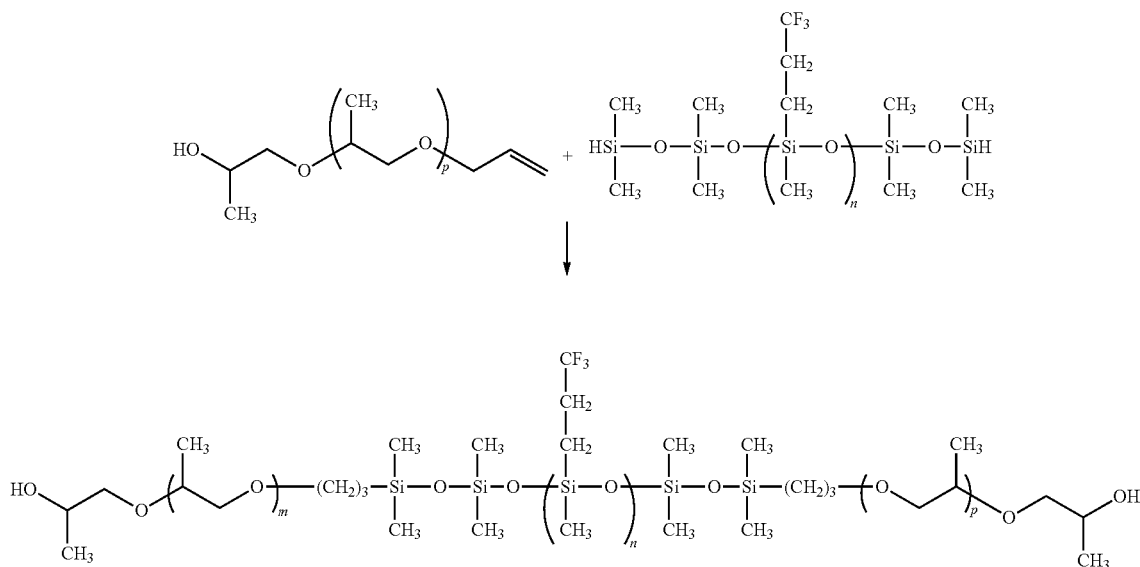
The synthetic procedure is as follows:

Step 1:



To a 4 neck separable flask fitted with mechanical stirrer, was added 40 g of Silanol terminated poly(trifluoropropyl methylsiloxane) (FMS-9922 from Gelest Inc.) and this was mixed with 50 ml of toluene and fitted with a continuous flush of Nitrogen. To the reaction mixture 7.57 g of dimethyl chlorosilane (DMCS, from Sigma Aldrich) was added slowly over about 20 minutes keeping the temperature of the mixture constant at 30° C. With each addition of dimethyl chlorosilane, the mixture became hazy but cleared in a short period of time. Once the addition of dimethyl chlorosilane was complete, the mixture was heated to 90° C. for 3 hours. The reaction was then washed with excess water several times to reduce the acidity of the mixture. The resulting mixture was dried over silica gel, filtered and vacuumed to remove solvent and traces of water at 65° C. overnight. A clear fluid was then obtained with a very strong Si—H band in infra red spectroscopy (IR) at 2130 cm<sup>-1</sup>, which confirms the reaction. GPC analysis showed the molecular weight to be 1200 g/mol.

Step 2:

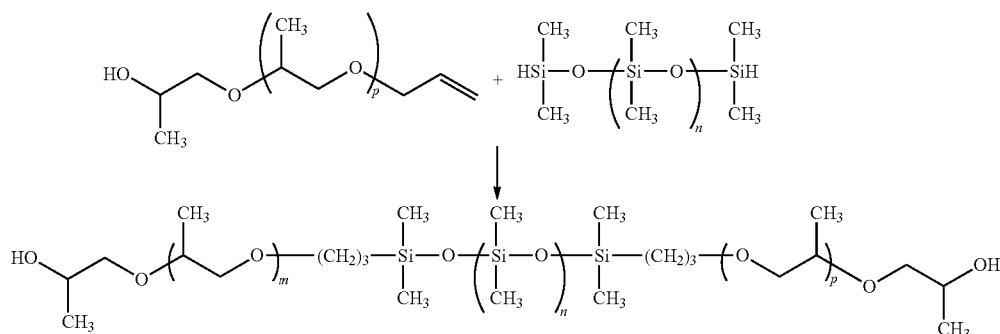


## 23

To 90 ml of reagent grade toluene in a 4 neck separable flask fitted with mechanical stirrer, 46.67 g of Allyl terminated poly(propylene glycol) (MW=700 g/mol, Jiangsu GPRO Group Co.) was added and then heated to reflux. Then 40 g of Hydride terminated FMS-9922 was dissolved in 50 ml of reagent grade toluene and the temperature raised to around 90° C. To the reaction mixture 2 drops of hexachloroplatinic (IV) acid (0.01M H<sub>2</sub>PtCl<sub>6</sub> from Sigma) solution in isopropanol (by Merck) was then added. After this catalyst solution had been added, the mixture was refluxed for 1 hour and the solvent distilled off in order to get the final product. The reaction was followed by H-NMR and gel permeation chromatography (GPC) confirmed the final molecular weight to be 2700 g/mol.

TABLE 1

Resulting polymer block ratios Stoichiometric ratios for reaction product:			
Polymer block			
	PO m	F—SiO n	PO p
Ratio	11	9.7	11



## 24

## Example 2

### Synthesis of Aliphatic Linked Dimethylsiloxane Based Triblock Copolymer Pre-Soft-Segment

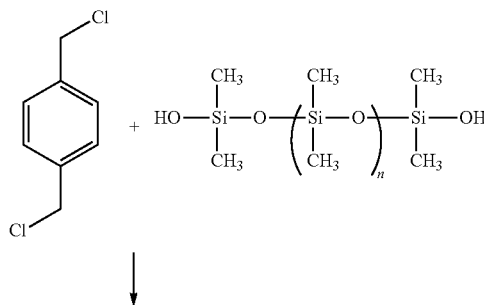
To 130 ml of reagent grade toluene in a separable flask fitted with a mechanical stirrer, was added 64 g of allyl terminated polypropylene glycol (MW=700 g/mol, Jiangsu GPRO Co.) and both were mixed and heated to reflux. Then 40 g of hydride terminated poly(dimethyl siloxane) (Silmer H Di 10 by Siltech Corp.) was dissolved in 50 ml reagent grade toluene and the temperature raised to around 90° C. To this reaction mixture 2 drops of hexachloroplatinic(IV) acid (0.01M H<sub>2</sub>PtCl<sub>6</sub> from Sigma) solution in isopropanol was added. After this catalyst solution was added, the mixture was refluxed for 1 hour and then the solvent was distilled off in order to get the final product. The reaction was followed with H-NMR and gel permeation chromatography (GPC) confirmed the final molecular weight of the product to be 2300 g/mol.

TABLE 2

Polymer block ratios Stoichiometric ratios for reaction product:			
Polymer block			
	PO m	SiO n	PO p
Ratio	11	11	11

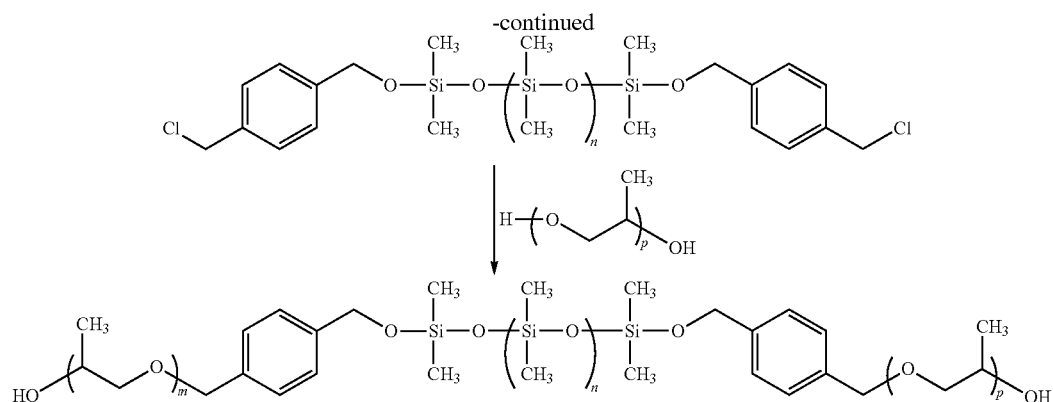
## Example 3

### Synthesis of Aromatic Linked Siloxane Based Triblock Copolymer Pre-Soft-Segment



25

26



To a 100 ml separable flask fitted with a mechanical stirrer, 15 g of hydroxy terminated polydimethyl siloxane (DMS-S14 from Gelest Inc.) was added along with 5.36 g of dichloro *p*-xylene (from Sigma) and 0.0089 g of Copper(II) acetylacetonate ( $\text{Cu}(\text{Acac})_2$  from Sigma). The reaction mixture was refluxed at  $110^\circ\text{C}$ . for 5 hrs. At this point, 19.77 g of hydroxy terminated polypropylene glycol (from Sigma) was added dropwise and the reaction mixture was then refluxed for another 15 hr. The progress of reaction was followed by  $^1\text{H}$ -NMR and the final molecular weight, determined by gel permeation chromatography (GPC), was 3000 g/mol.

H-NMR Analysis:

Solvent used for  $^1\text{H}$ -NMR analysis is  $\text{CDCl}_3$ .

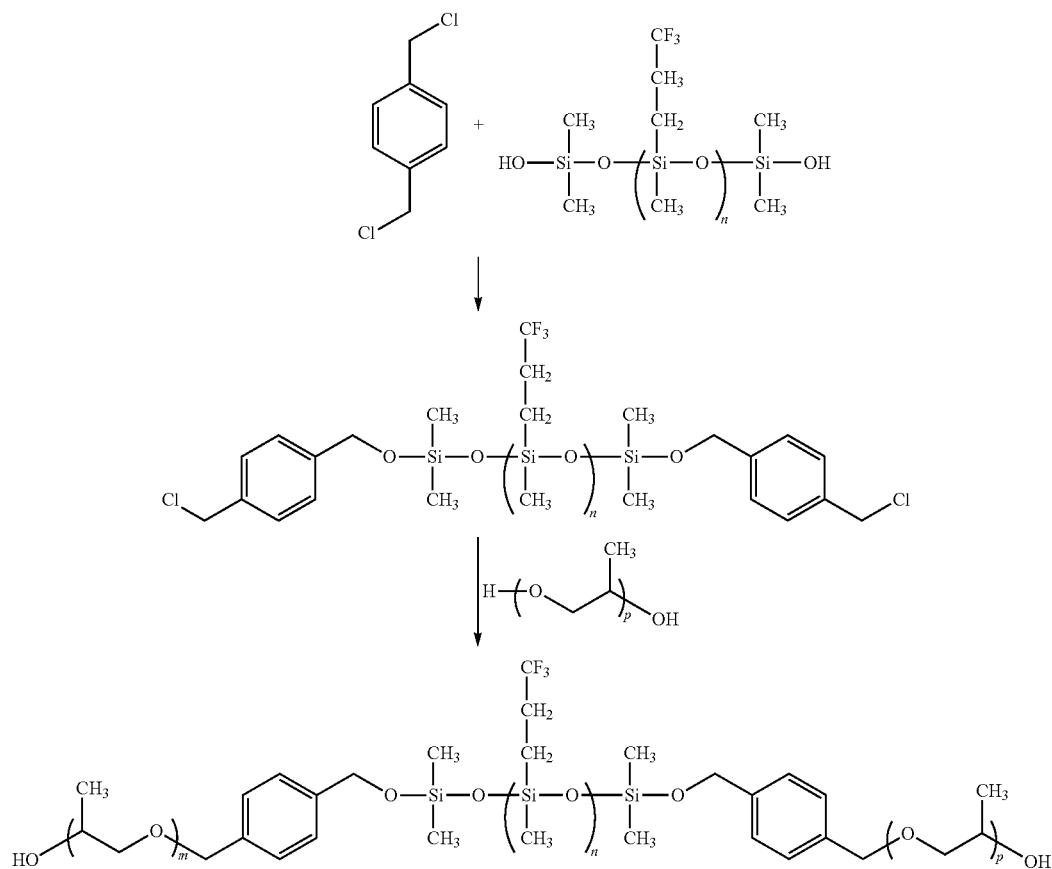
Aromatic H=7.25-7.45 ppm,  $-\text{CH}_2-$ =4.5-4.6 ppm,  $-\text{CH}_3$  (of PPO)=1-1.4 ppm,  $-\text{CH}_2-$  (of PPO)=3.2-3.8 ppm,  $-\text{OH}$  (of PPO)=3.8-4 ppm,  $-\text{CH}_3$ (silanol)=0.5-0.8 ppm.

TABLE 3

	Resulting polymer block ratios Stoichiometric ratios for reaction product:		
	Polymer block		
	PO m	SiO n	PO p
Ratio	14	15.5	14

## Example 4

### Synthesis of Aromatic Linked Fluorosiloxane Based Triblock Copolymer Pre-Soft-Segment



## 27

To a 100 ml separable flask fitted with a mechanical stirrer, 15 g of hydroxy terminated polytrifluoromethyl siloxane (FMS-9922, Gelest inc.) was added along with 5.9 g of dichloro p-xylene and 0.0098 g of copper(II) acetylacetonate (Cu(Acac)<sub>2</sub> from Sigma). The reaction mixture was refluxed at 110° C. for 5 hrs. At this point, 21.75 g of hydroxy terminated polypropylene glycol (from Sigma) was added dropwise to the reaction mixture. The reaction was refluxed for another 15 hr. The progress of reaction was followed by <sup>1</sup>H-NMR analysis and the molecular weight, determined by gel permeation chromatography (GPC), was 3100 g/mol.

<sup>1</sup>H-NMR Analysis:

Solvent used for H-NMR analysis is CDCl<sub>3</sub>.

Aromatic <sup>1</sup>H=7.25-7.45 ppm, —CH<sub>2</sub>=4.5-4.6 ppm, —CH<sub>3</sub> (of PPO)=1-1.4 ppm, —CH<sub>2</sub> (of PPO)=3.2-3.8 ppm, —OH (of PPO)=3.8-4 ppm, —CH<sub>3</sub>(silanol)=0.5-0.8 ppm.

TABLE 4

Polymer block ratios			
Stoichiometric ratios for reaction product:			
	Polymer block		
	PO m	FSiO n	PO p
Ratio	14	9.2	14

## Example 5

## Preparation of Water Blown Foam

The pre-soft segments prepared can be described as having polymer block ratios which are numerically represented by the letters m, n and o for the constituents PO/SiO/PO respectively. The triblock copolymers prepared in Examples 1 and 2 with specific m, n, o ratios were formulated into polyurethane/urea foams as illustrated by Table 7.

The process for preparing the foam was a two-step procedure. The following describes the method of manufacture of the first product in Table 7. The same procedure was used to prepare other foams as described by Table 8.

Step 1) Firstly a mixture was made with 0.041 g of DABCO LV-33 (Airproducts), 0.120 g of bismuth neodecanoate (Bicat 8108M from Shepherd chemicals), 0.467 g of diethanol amine (DEOA, from Sigma), 7.917 g of synthesized block copolymer, 0.200 g water and 0.1 g of surfactant (Niax L-618 from Airproducts) in a plastic flat bottomed container. This is then thoroughly mixed manually for 30 sec until a homogenous mixture was obtained.

Step 2) To the above mixture, 15 g of a diisocyanate prepolymer (PPT 95A Airproducts) was added. This was then thoroughly mixed by a mechanical stirrer for about 5 seconds. The material was then molded and cured at 70° C. for 2.5 hours and post cured at 50° C. for another 3 hours.

TABLE 5

Formulation details for foam					
Formulation Identification	Polymer block (PO/SiO/PO) Ratio m:n:p	DABCO	BICAT	DEOA	H <sub>2</sub> O
VF230209A	11:11:11	0.0325	0.015	0.40	1.0
VF090309B	11:9:11	0.0325	0.015	0.40	1.0

## 28

## Example 6

## Comparative Example of Formulation of Water Blown Foam from Triblock Copolymer Pre-Soft Segment and Individual Homopolymers

Polyurethane/urea polymer foams from Example 5 were compared to foams made from the stoichiometric equivalent homopolymer soft segments. The foams with homopolymer based soft segments (VF130309 and VF190309) shown in FIG. 4 were produced as follows (VF130309):

Step 1) Firstly a mixture was made with 0.041 g of DABCO LV-33 (Airproducts), 0.120 g of bismuth neodecanoate (Bicat 8108M from Shepherd chemicals), 0.467 g of diethanol amine (DEOA, from Sigma), 3.056 g of poly (dimethyl siloxane) diol (DMS-s14 Gelest Inc.), 1.633 g of polypropylene oxide (Mw=700 g/mol), 0.200 g water and 0.1 g of surfactant (Niax L-618 from Airproducts). These were added to a plastic flat bottomed container and were thoroughly mixed manually for 30 sec until a homogenous mixture was obtained.

Step 2) To the above mixture, 15 g of a diisocyanate prepolymer (PPT 95A Airproducts) was added. This was then thoroughly mixed by a mechanical stirrer for 5 seconds. The material was then molded and cured at 70° C. for 2.5 hours and post cured at 50° C. for another 3 hours.

The foams in this example were made into dumbbell shapes for tensile testing. FIGS. 4 and 5 illustrate the difference in mechanical behaviour between the comparative materials indicating a favourable lowering in modulus for the triblock copolymer pre-soft-segments.

## Example 7

## Comparative Stability of Triblock Copolymer Soft Segment Versus Homopolymer Soft Segment

Tensile test specimens were prepared in the same manner to the materials used in Example 4 and were subjected to accelerated aging in simulated gastric fluid (as per United States Pharmacopeia, "USP"). The materials produced with the pre-synthesised triblock copolymer soft segments resulted in substantially improved mechanical stability in gastric fluid as compared to the urethane/urea linked homopolymer equivalent as illustrated in FIG. 5. This facilitates the use of such materials for prolonged periods in digestive and more specifically gastric environments.

## Example 8

## Preparation of Water Blown Foams

Several water blown polyurethane/urea foams were also produced with varying PO/EO/SiO polymer block ratios. The process for preparing the foam as described above was used.

TABLE 6

Water blown formulations incorporating siloxane containing copolymer pre-soft-segments.					
Polymer block ratio (PO/EO/SiO) m:n:p		DABCO	BICAT	DEOA	H <sub>2</sub> O
41.5:8.3:0.5		0.114	0.022	0.22	2.72
40.2:7.8:0.5		0.114	0.022	0.22	2.72
37.5:7:0.5		0.114	0.022	0.22	2.72

29

TABLE 6-continued

Water blown formulations incorporating siloxane containing copolymer pre-soft-segments.				
Polymer block ratio (PO/EO/SiO) m:n:p	DABCO	BICAT	DEOA	H <sub>2</sub> O
33.5:5.7:0.5	0.114	0.022	0.22	2.72
29.6:4.4:0.5	0.114	0.022	0.22	2.72
21.6:1.8:0.5	0.114	0.022	0.22	2.72
19:1:0.5	0.114	0.022	0.22	2.72
29.6:4.5:1.1	0.114	0.022	0.22	2.72

The results from the formulations described in Table 6 are shown in Table 7.

TABLE 7

Results from mechanical testing of foams from Table 5		
Polymer block ratio (PO/EO/SiO) m:n:p	% Elongation	Tensile Strength (N)
41.5:8.3:0.5	233	0.46
40.2:7.8:0.5	243	0.31
37.5:7:0.5	237	0.3
33.5:5.7:0.5	260	0.23
29.6:4.4:0.5	320	0.23
21.6:1.8:0.5	497	0.23
19:1:0.5	462	0.22
29.6:4.5:1.1	437	0.29

## Example 9

## Use Example

Devices for use in the gastrointestinal system have historically not been made from specifically designed materials. Off the shelf materials used for application in the corrosive environment of the stomach have limited biostability and generally lose their functionality after a short time.

The foam of the invention can be used for production of a valve of the type described in our US2007-0198048A, the entire contents of which are incorporated herein by reference. The valve has an open position and a closed position. The valve will have a proximal end and a distal end. The valve material can open from the proximal direction when the action of swallowing (liquid or solid) stretches an orifice by between 100% and 3000% in circumference. The open orifice optionally closes non-elastically over a prolonged period of time, thus mimicking the body's natural response. The duration taken to close may be between 2 and 15 sec. The material can stretch to between 100%-300% from the distal direction when gas, liquid or solids exceeds a pre-determined force of between 25 cmH<sub>2</sub>O and 60 cmH<sub>2</sub>O. In some embodiments, the material absorbs less than 15% of its own mass of water at equilibrium. In some embodiments, the material loses (leaches) less than 3% of its own mass at equilibrium in water or alcohol. In some embodiments, the material loses less than 10% of its tensile strength when immersed in a simulated gastric fluid at pH 1.2 for 30 days. In some embodiments, the valve material loses less than 25% of its % elongation when immersed in a simulated gastric fluid at pH 1.2 for 30 days.

## Example 10

## Valve Functional Testing

The healthy lower esophageal sphincter (LES) remains closed until an individual induces relaxation of the muscle by

30

swallowing and thus allowing food to pass in the antegrade direction. Additionally when an individual belches or vomits they generate enough pressure in the stomach in the retrograde direction to overcome the valve. An anti-reflux valve must enable this functionality when placed in the body, thus a simple functional test is carried out to assess performance.

It has been reported that post fundoplication patients have yield pressures between 22-45 mmHg and that most of the patients with gastric yield pressure above 40 mmHg experienced problems belching. See *Yield pressure, anatomy of the cardia and gastro-oesophageal reflux*. Ismail, J. Bancewicz, J. Barow British Journal of Surgery. Vol: 82, 1995, pages: 943-947. Thus, in order to facilitate belching but prevent reflux, an absolute upper GYP value of 40 mmHg (550 mmH<sub>2</sub>O) is reasonable. It was also reported that patients with visible esophagitis all have gastric yield pressure values under 15 mmHg, therefore, there is good reason to selectively target a minimum gastric yield pressure value that exceeds 15 mmHg. See Id. An appropriate minimum gastric yield pressure value would be 15 mmHg+25% margin of error thus resulting in a minimum effective valve yield pressure value of 18.75 mmHg or 255 mmH<sub>2</sub>O.

The test apparatus consists of a 1 m high vertical tube as shown in FIG. 7, to which is connected a peristaltic pump and a fitting that is designed to house the valve to be tested.

The valve to be tested is placed in a water bath at 37° C. for 30 minutes to allow its temperature to equilibrate. Once the temperature of the valve has equilibrated it is then installed into the housing such that the distal closed end of the valve faces the inside of the test apparatus. The pump is then switched on at a rate of 800 ml/min to begin filling the vertical tube. The rising column of water exerts a pressure that forces the valve shut initially. As the pressure in the column rises the valve reaches a point where it everts and allows the water to flow through. This point, known as the yield pressure, is then recorded and the test repeated four times.

## Example 11

## Rationale for Accelerated Aging of Material

## Clinical Condition being Simulated

The lower oesophagus of a normal patient can be exposed to the acidic contents of the stomach periodically without any adverse side effects. However, patients with gastro esophageal reflux disease experience damage to the mucosa of the lower oesophagus due to increased exposure to the gastric contents. Exposure of the lower oesophagus to acidic gastric contents is routinely measured in the clinic using dedicated pH measurement equipment. A typical procedure involves measuring pH over a 24-hour period. The levels of acid exposure in pathological reflux disease patients is summarised in Table 8 from six clinical references. See DeMeester T R, Johnson L F, Joseph G J, et al. *Patterns of Gastroesophageal Reflux in Health and Disease Ann. Surg.* October 1976 459-469; Pandolfino J E, Richter J E, Ours T, et al. *Ambulatory Esophageal pH Monitoring Using a Wireless System Am. J. Gastro* 2003; 98:4; Mahmood Z, McMahon B P, Arfin Q, et al. *Results of endoscopic gastroplasty for gastroesophageal reflux disease: a one year prospective follow-up Gut* 2003; 52:34-9; Park P O, Kjellin T, Appeyard M N, et al. *Results of endoscopic gastroplasty suturing for treatment of GERD: a multicentre trial Gastrointest endosc* 2001; 53:AB115; Filipi C J, Lehman G A, Rothstein R I, et al. *Transoral flexible endoscopic suturing for treatment of GERD: a multicenter trial Gastrointest endosc* 2001; 53 416-22; and Arts J, Sloot-

31

maekers S Sifrim D, et al. *Endoluminal gastroplication (Endocinch) in GERD patient's refractory to PPI therapy Gastroenterology* 2002; 122:A47.

TABLE 8

Summary of acid exposure in patients with reflux disease			
Investigator	Number of patients	Details	% 24 h <pH 4
DeMeester	54	Combined refluxers	13.5
Pandolfino	41	Gerd	6.5
Mahmood	21	Gerd	11.11
Park	142	Gerd	8.5
Filipi	64	Gerd	9.6
Arts	20	Gerd	17
Average			11.035

## Key Clinical Parameters

Considering that the lower oesophagus is exposed to the acidic pH exposure time for an average of 11% of the measurement period, an accelerated aging methodology can easily be conceived. Constant exposure of a test material to the gastric contents (or USP Simulated Gastric Fluid—Reference USP Pharmacopeia) would represent an almost 10-fold increase in the rate of aging. Thus the time required to simulate one year of exposure of the lower oesophagus to the gastric contents is described by equation 1.

$$\left(\frac{11.035}{100}\right) \times 365 \text{ days} = 40.28 \text{ days} \quad \text{Equation 1}$$

## Clinical Rationale

Immersion of test specimens in USP Simulated gastric fluid for 40.27 days at 37° C. will approximate one year's exposure of the lower oesophagus to acidic gastric contents in a GERD patient's scenario.

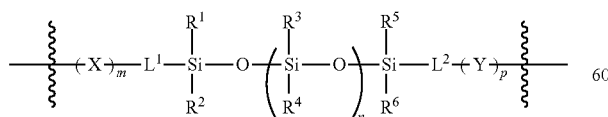
Simulated Exposure	Real Time
1 year	40.28 days
2 years	80.56 days
3 years	120.84 days

Results of accelerated stability of a valve prepared from a viscoelastic foam of the present invention are depicted in FIGS. 8A and 8b.

While we have described a number of embodiments of this invention, it is apparent that our basic examples may be altered to provide other embodiments that utilize the compounds and methods of this invention. Therefore, it will be appreciated that the scope of this invention is to be defined by the appended claims rather than by the specific embodiments that have been represented by way of example.

What is claimed is:

1. A triblock copolymer of formula I:



wherein:

each  $\text{---} \text{X} \text{---}$  represents a point of attachment to a urethane or urea linkage and the triblock copolymer is chemically interspersed between the urethane or urea linkage;

32

each of X and Y are both the same, an each of X and Y is independently an ether, an ester, a carbonate, or a fluorohydrocarbon, or mixture thereof;

each of R<sup>1</sup>, R<sup>2</sup>, R<sup>3</sup>, R<sup>4</sup>, R<sup>5</sup> and R<sup>6</sup> is independently selected from one or more of R, OR, —CO<sub>2</sub>R, a fluorinated hydrocarbon, a polyether, a polyester or a fluoropolymer;

each R is independently hydrogen, an optionally substituted C<sub>1-20</sub> aliphatic group, or an optionally substituted group selected from phenyl, 8-10 membered bicyclic aryl, a 4-8 membered monocyclic saturated or partially unsaturated heterocyclic ring having 1-2 heteroatoms independently selected from nitrogen, oxygen, or sulphur, or 5-6 membered monocyclic or 8-10 membered bicyclic heteroaryl group having 1-4 heteroatoms independently selected from nitrogen, oxygen, or sulfur;

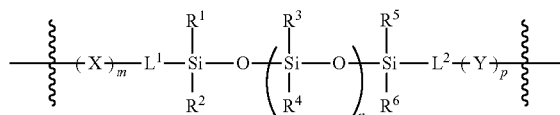
each of m and p is independently 2 to 100;

each of L<sup>1</sup> and L<sup>2</sup> is independently a bivalent C<sub>1-20</sub> hydrocarbon chain wherein 1-4 methylene units of the hydrocarbon chain are optionally and independently replaced by —O—, —S—, —N(R)—, —C(O)—, —C(O)N(R)—, —N(R)C(O)—, —SO<sub>2</sub>—, —SO<sub>2</sub>N(R)—, —N(R)SO<sub>2</sub>—, —OC(O)—, —C(O)O—, or a bivalent cycloalkylene, arylene, heterocyclene, or heteroarylene, provided that neither of L<sup>1</sup> nor L<sup>2</sup> comprises a urea or urethane moiety; and

each of L<sup>1</sup> and L<sup>2</sup> is independently a bivalent C<sub>1-6</sub> alkylene chain wherein at least one methylene unit of the chain is replaced by —O— and at least one methylene unit of the chain is replaced by a bivalent arylene.

2. The copolymer according to claim 1 wherein each of L<sup>1</sup> and L<sup>2</sup> is independently —OCH<sub>2</sub>-phenylene-, —OCH<sub>2</sub>CH<sub>2</sub>-phenylene-, —OCH<sub>2</sub>CH<sub>2</sub>-phenylene-CH<sub>2</sub>—, or —OCH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>-phenylene-.

3. A triblock copolymer of formula I:



wherein:

each  $\text{---} \text{X} \text{---}$  represents a point of attachment to a urethane or urea linkage and the triblock copolymer is chemically interspersed between the urethane or urea linkage;

each of X and Y are both the same, and each of X and Y is independently an ether, an ester, a carbonate, or a fluorohydrocarbon, or mixture thereof;

each of R<sup>1</sup>, R<sup>2</sup>, R<sup>3</sup>, R<sup>4</sup>, R<sup>5</sup> and R<sup>6</sup> is independently selected from one or more of R, OR, —CO<sub>2</sub>R, a fluorinated hydrocarbon, a polyether, a polyester or a fluoropolymer;

each R is independently hydrogen, an optionally substituted C<sub>1-20</sub> aliphatic group, or an optionally substituted group selected from phenyl, 8-10 membered bicyclic aryl, a 4-8 membered monocyclic saturated or partially unsaturated heterocyclic ring having 1-2 heteroatoms independently selected from nitrogen, oxygen, or sulphur, or 5-6 membered monocyclic or 8-10 membered bicyclic heteroaryl group having 1-4 heteroatoms independently selected from nitrogen, oxygen, or sulfur;

each of m and p is independently 2 to 100; and wherein each of L<sup>1</sup> and L<sup>2</sup> is independently a bivalent C<sub>1-6</sub> alkylene chain wherein at least one methylene unit of the

**33**

chain is replaced by —O— and at least one methylene unit of the chain is replaced by a bivalent arylene.

4. The triblock copolymer of claim 3 wherein each of L<sup>1</sup> and L<sup>2</sup> is independently —OCH<sub>2</sub>-phenylene-, —OCH<sub>2</sub>CH<sub>2</sub>-phenylene-, —OCH<sub>2</sub>CH<sub>2</sub>-phenylene-CH<sub>2</sub>—, or —OCH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>-phenylene-.

\* \* \* \* \*

**34**